BULLETIN

OF

THE JOHNS HOPKINS HOSPITAL.

Vol. IX.—No. 85.] BALTIMORE, APRIL, 1898. [Price, 15 Cents.

CONTENTS.

	PAGE.
Miniature Hammers and the Suture of the Bile Ducts. By W. S. Halsted, M. D.,	67
University Education. By Michael Foster,	69
The Results of the Intra-tracheal Inoculation of the Bacillus Diphtheriæ in Rabbits. By Simon Flexner, M. D., and H. B. Anderson, M. D.,	72
The Bacteriology of Pertussis. By Henry Koplik, M. D.,	79
Supplementary Report on the Sterilization of Instruments by Formaldehyde. By H. O. Reik, M. D.,	82
Correspondence: Does Wilhite's Story of the Negro Boy Incident in the Discovery of Anæsthesia "lack Probability"? Letters from J. O. Wilhite, M. D., and Hugh H. Young, M. D.,	83
Notes on New Books,	88

MINIATURE HAMMERS AND THE SUTURE OF THE BILE DUCTS.*

By W. S. Halsted, *Professor of Surgery in the Johns Hopkins University and Surgeon-in-Chief to the Johns Hopkins Hospital.*

The surgery of the common bile duct is still in its infancy. "Suture of the thickened duct is difficult enough, and suture of the normal duct out of the question," says one. "It is not worth while to exercise such great care in sewing up a slit in the common bile duct, for it is almost impossible to prevent leakage, and a little additional leakage can do no harm if one drains," says another. "Wait until the common bile duct dilates and thickens before venturing to open it," say all surgeons.

"Ein normaler Ductus choledochus ist ein ausserordentlich dünnwandiges Gebilde; eine Längswunde in demselben exakt zu vernähen, durfte technisch ausserordentlich schwierig sein, zumal man durch Einstülpung der Wundränder leicht das Lumen des Kanales zu sehr verengen kann. Zum Glücke erweitert sich der Ductus choledochus bei Eintritt von irgendwie grösseren Steinen alsbald, seine Wandung wird dicker, so dass Incision und Naht meist leicht gelingen."†

"Beim dritten Act, habe ich die Schwierigkeit des Nahtverschlusses der Incision des Choledochus, welche in 2 Fällen überhaupt unmöglich war, kennen gelernt, die Nützlichkeit der Tamponnade eingesehen, sobald die Choledochotomie für sich allein ausgeführt oder mit der Cystectomie verbunden wurde."* "Eine Choledochotomie rechnet er [Kümmell†] zu den technisch schwierigsten Operationen."‡

To close an incision in the normal ductus communis choledochus has been considered so impracticable, not to say impossible, and the result of the suture, so far as the suture itself is concerned, even of the abnormally thickened duct so uncertain, that it is the practice of all surgeons to wait weeks or months or even years for the duct to dilate and thicken rather than interfere promptly in cases of obstruction of the common bile duct by stone.

It is perhaps justifiable to "give nature a chance" to expel the stone, but the operation should never be postponed solely for the sake of giving the duct time to become thicker. I know from operations upon dogs and man that the normal bile ducts can be sutured easily, accurately, almost infallibly, and without danger of leakage or constriction.

We are all more or less acquainted with the more evident dangers of postponing choledochotomy when it is indicated; the deep jaundice, the retarded blood coagulation and the consequent danger from hemorrhage, whether an operation is performed or not; the cirrhotic hypertrophy of the liver and the concomitant hemorrhages into stomach and intestines, the

*Presented at the Johns Hopkins Hospital Medical Society, December 13, 1897.

†Riedel. Chirurgische Behandlung der Gallensteinkrankheit, p. 115. Handbuch der Speciellen Therapie innerer Krankheiten, Bd. iv.

*Kehr. Ein Rückblick auf 209 Gallensteinlaparotomieen. Arch. für Klin. Chirurgie, Bd. liii, Heft 2, p. 375.

†Mittheilungen aus den Hamburgischen Staatskrankenanstalten, 1897, Bd. 1, Heft 2.

‡Ref Tschmarke, Centralblatt für Chirurgie, 1898, No. 5, p. 134.

acute or chronic inflammation of the bile passages; toxæmia, cholæmic or infectious, and the interference with metabolism, more serious, perhaps, in its remoter consequences than we have estimated. And when at last the operation is resorted to the patient is perhaps so weak that the surgeon might well wish that he had interfered earlier.

The duct lies in a deep hole, at a great distance from the surface, and is covered by the liver, which is usually enlarged in the cases which we are considering, and which, if very large or very small, may embarrass the operator exceedingly. The suggestion of Dr. Fred. Lange to cut through one or two ribs and the diaphragm when the liver is very large we have found invaluable. And not only when the liver is large have we profited by this hint; for once when it was small and high up under the ribs, the duct, carried up with it, was perhaps even less accessible than in the cases complicated with large liver.

Once then because of a small liver, and several times because the livers were large, have I divided ribs and diaphragm, and each time with gratifying results. When operating upon the bile passages of dogs I divide two or three ribs and the underlying diaphragm as a matter of routine. Cutting through a few ribs and the diaphragm on the left side enabled me to remove a large and very adherent tuberculous kidney.

With the little hammers which I am describing, or with a similar contrivance, I have five times sutured the common bile duct in dogs, and twice the common duct and once the cystic duct in the human subject. Two of the dogs referred to were operated upon last spring and observed during the summer and part of the autumn.

Dog 1. June 24, 1897. Long incision in common bile duct sutured over an aluminum rod with six mattress sutures of fine black silk. The wall of the duct was so thin that all of the stitches necessarily penetrated it. The silk itself was thicker than the wall. I intentionally turned in a great deal of the wall, wishing to temporarily occlude the lumen of the duct; and having withdrawn the rod and tied the sutures, I was impressed with the thread-like appearance of the duct and thought that I had perhaps totally occluded it. The dog was apparently as well as usual in a day or two and was observed all summer. At no time was he jaundiced, nor did he seem to be in the least inconvenienced by the operation.

Oct. 1st. Dog killed with ether. Autopsy. Except for the few silk threads in the tissues there was little to evidence the operation.

Dog 2. June 24, 1897. Through an incision into the ductus communis choledochus a small shot not quite large enough to occlude the lumen of the duct was introduced. The duct was sutured with mattress sutures over an aluminum rod as in the preceding case.

The aluminum rods, of several sizes, were flexible and were bent to suit the case just before using. I was very much pleased with the rods, because they made not only possible but very easy what hitherto had been considered too difficult to attempt. The rods suggested to me the rubber bags for intestinal suture which I have already described.*

* Philadelphia Med. Journ., Jan. 8, 1898, and The Johns Hopkins Hospital Bulletin, Feb., 1898.

The little hammers which I now use answer the purpose better than the rods. Within the past three weeks I have twice used the hammers on the human subject. If properly employed they convert one of the most difficult operations in surgery into quite a simple one. The hammers are of sizes (vid. Figs. 4 and 5) to meet all cases, from the normal duct in a dog to a much dilated human duct.

To Use the Hammer in Suture of the Common Bile Duct.

It is not necessary to dissect the duct from its bed, but the wall of the duct should be clearly exposed at the site selected for the incision. I usually incise the common bile duct near its duodenal end because the diverticulum of Vater can be more thoroughly explored through an incision at this end of the duct, and because it is easier to suture this end than the other or cystic end of the common bile duct.

Before incising the duct, two presection stitches, to serve as retractors, should be taken. These stitches, which are subsequently removed, should enter the lumen of the duct. They are placed close together and the incision into the lumen of the duct is carried between them (vid. Fig. 1).

The stone having been removed and the gall passages thoroughly searched with probe and fingers, the retractor threads are drawn apart and a hammer of the proper size introduced (vid. Fig. 2).

The duct is then gently raised from its bed and drawn towards the operator (vid. Fig. 3) by the hammer, the head of which is of course longer than the incision.

Mattress stitches are then applied as shown in Fig. 3; one over the heel behind the handle of the hammer, and the others in front of the very delicate handle. This beautiful drawing was made from the subject and depicts accurately the parts concerned in this stage of the operation.

Although the finest possible needles and silk are used the stitches necessarily perforate the wall of the normal duct. No harm results from this perforation, however, for the normal duct practically always and the thickened duct usually is sterile, and the stitches very soon cut their way out of the lumen and out of the wall of the duct and lie free in the adventitious tissues.

The silk which we use is very much finer than the artist supposed when he made the drawings, and the needles, made for us by Wülfing-Luer, of Paris, have a split eye and are almost as fine as the silk itself. One should have a needle-holder especially made and reserved for these needles. If such a needle-holder is used for coarser work it will soon be ruined.

I have been asked why the handle is not placed in the middle of the hammer. It is placed as near one end as practicable, to enable the operator to introduce the hammer through as small an incision as possible, an incision not longer than about ha the circumference of the hammer.

The Advantages of the Hammer.

1. The duct to be sutured can be drawn towards the incision in the anterior abdominal wall and within easy reach of the operator; it can also be manipulated nicely by the hammer.

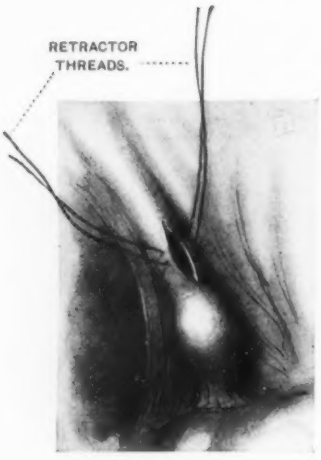


FIG. 1.

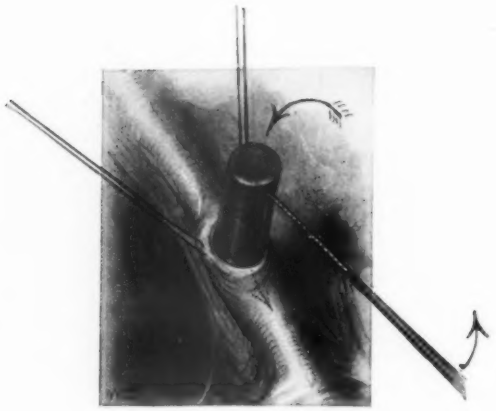


FIG. 2.

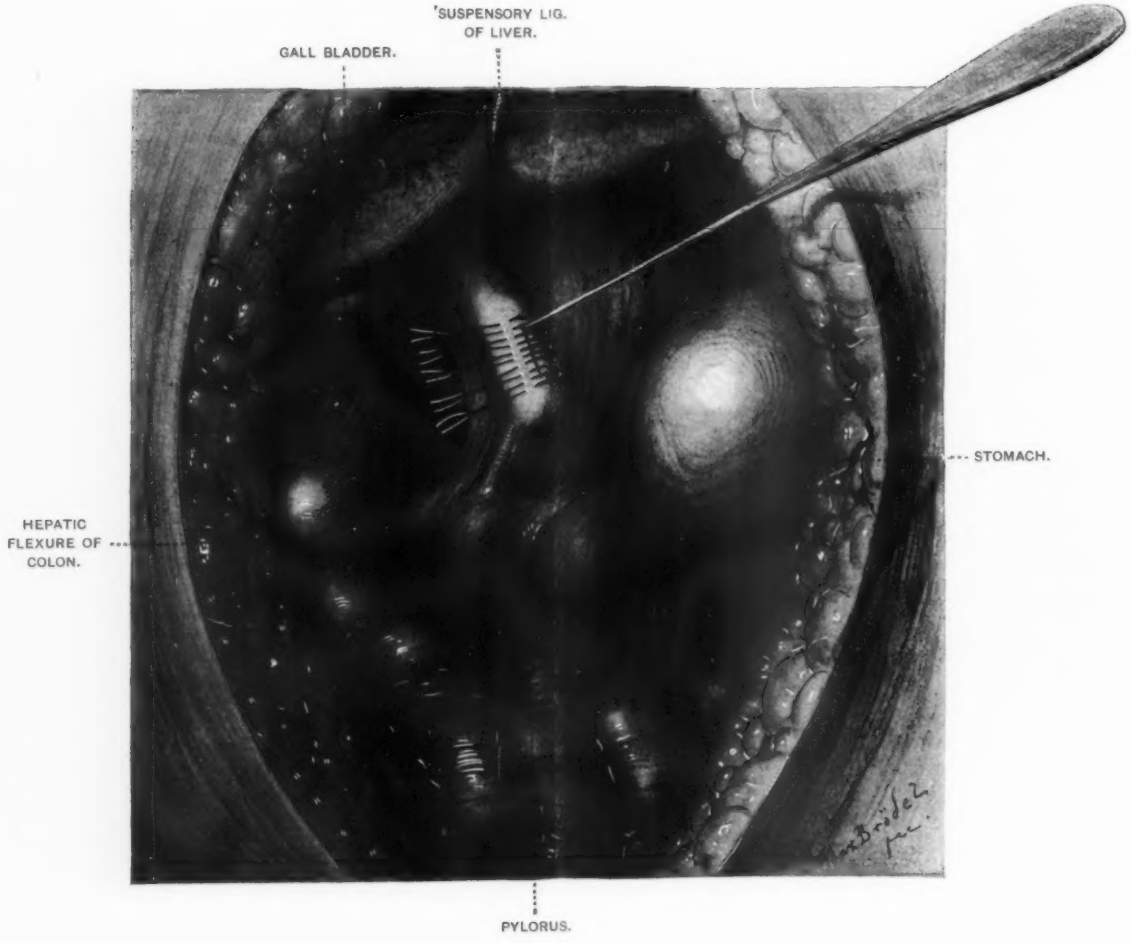


FIG. 3.

ACTUAL LENGTH.

FIG. 4.

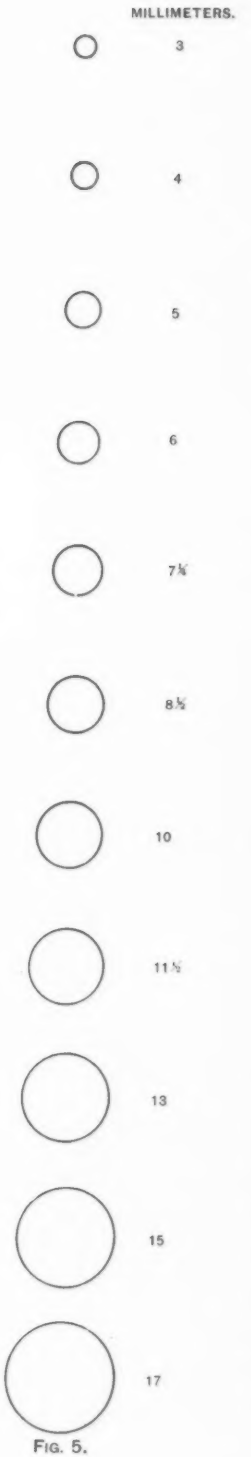


FIG. 5.

2. The duct, whether normal or thickened and dilated, is gently expanded by the hammer; hence the stitches can be taken with great accuracy and without fear of including the opposite wall or of occluding the lumen of the duct.

3. The operation is a very clean one, because the hammer blocks the duct and this prevents the escape of its contents and the contents of the gall bladder.

4. With the hammer, wounds of thin normal ducts can be easily and almost infallibly sutured, and hence the surgeon may, if he chooses, fearlessly operate upon the common duct as soon as the obstruction takes place.

The sewing of the thickened and dilated ducts is also greatly facilitated by the employment of the hammer.

UNIVERSITY EDUCATION.

By Michael Foster, *University of Cambridge, England.*

[*Address delivered at the Johns Hopkins University, Baltimore, October* 11, 1897.]

[President Gilman introduced Prof. Foster in the following words: "I have the pleasure of presenting to this assembly the distinguished physiologist, Dr. Michael Foster, Professor in the University of Cambridge, England, and one of the secretaries of the Royal Society of London. He comes at the invitation of the Medical Faculty of this University, and it is an auspicious opening of the year that brings him here; auspicious not only by his presence, but by the beautiful weather that has favored us and by the large number of students now enrolled in the medical department.

I can say of him that though his face is not familiar, a very large number of the young men and ladies present feel that they have already taken him by the hand, as his manual of physiology has been in use among us from the beginning of the Johns Hopkins University. You will be glad to be reminded that when biological studies were introduced here it was through the agency of Dr. H. Newell Martin, who had been a pupil of Dr. Foster's, first in London and afterwards in Cambridge. During the past score of years by correspondence we have maintained the most friendly relations, and we rejoice in this favorable opportunity to hear what he may say upon University Education."]

The Johns Hopkins University, which has done me the honor to ask me to say a few words on this occasion, is, although already distinguished, a new and young university. I can remember well its beginning, and as Dr. Gilman has hinted, I may claim to have taken some small part in its birth. When I moved in 1870 from London to Cambridge, I took with me a bright lad of whose ability and industry I had already taken notice. At Cambridge he became my right hand man, and I had some hopes that I should long have his help; but President Gilman appeared upon the scene, and his influence was so strong that I felt that my own interests were not to be considered, and that I ought to send that favorite across the waters to occupy the first chair of biology in this new university. Although the memories of him whom I need scarcely name, Henry Newell Martin, are tinged with melancholy, still I feel that this university must always look back with pride and affection on the work which he has done in this country, and in this affection and pride I claim a small share for myself.

Your university is a new one. I come from a very old one; one which was founded six hundred years ago, which has lived through all those centuries, and which, though it has some of the charms, has also some of the evils of antiquity. The traditions of the past weigh heavy upon us. When we attempt to stretch our limbs to meet the new needs of new times we find some old written law, some well established prejudice, some vested interest preventing our full development. You are a new university; and although I have purposely refrained from refreshing my mind as to the exact status of your regulations and as to how far you may have already entangled yourselves in the toils of enactments, still I will take it for granted that you differ from us in the freedom with which you can move forward towards the needs of the coming times; and I think perhaps I could not do better at the present moment than to use the opportunity offered me to take my old university as a text and to draw from it and its history some few plain reflections which I hope may be practical and useful with regard to the conduct of universities. Although I understand that I have been especially invited by the medical faculty, I will take leave to treat only of general things, since the welfare of the medical faculty is bound up in that of the whole university.

The morphologists tell us we can learn much by studying the embryo, and something perhaps may be learned by looking back at this old University of Cambridge in the days of long ago—in the days when it too was a relatively young university. Things were very different then from what they are now. The dimly lighted streets or alleys in which the students lived were an emblem of the whole university. There was little outward show of glory then, there were no beautiful buildings, few books, and each student's duty was, in part, to listen to the lecture, to the reading of something which was written, but which he could not see with his own eyes. In spite of all these difficulties there were certain features of the university of that time which I trust I may say have been, with some little wavering here and there, maintained since, and which I cannot help thinking have contributed in very large measure to make it what I may venture to call it, a famous and great university.

One of the most striking features of the attitude of both students and teachers at that early time was that they recognized in the training of the university a preparation for practical life. There were at that time three main occupations in which learning was of practical use; and in correspondence to those three occupations there were established the three great faculties of the university, the faculty of theology, the faculty of law and the faculty of medicine. And, if one reads what those men of old wrote concerning what they thought ought

to be done in the university, one is very much impressed by the conviction which they had that the teaching should be an earnest preparation for practical life. If it soon became necessary to establish a fourth faculty, the faculty of arts, that was simply as a faculty preparatory to the others, as one supplying the first steps for and leading up towards the knowledge which should be of use in practical life; and it is worth noting that although they called that faculty the faculty of arts, and although the acquisition of the Latin language was one of the chief studies of that faculty, necessarily so because all the instruction which could be given was given in that tongue, among what they called the arts were the beginnings of the kind of knowledge which we now call science.

Another feature of the university life of those early times was the very strong feeling that the work of the university consisted not in the mere acquisition of knowledge, but in the training of the mind. The amount of knowledge which they had for distribution was very limited; but they used that small stock of knowledge to the very best of their ability, as the means of awakening the minds of the students and training them for thinking and arriving at conclusions. This is seen even in what they called at that time examinations, though the word then had a very different meaning from what it has now; there were then no written examinations, there was not that demand on paper so characteristic of modern times, and that great necessity of modern civilization, the waste-paper basket, was unknown. The examiners went quietly to work to ascertain in the most sure way whether a student had profited by what he had listened to. Instead of having two examiners for some hundreds of students, they appointed nine to each student; and these went in with him and out with him until they satisfied themselves that he knew something and had gathered something from what had been told him. And then as a final test they put him on the "stool" and made him debate in public, the test being used in such a way as to bring out his stock of knowledge, and especially his power of using it and of showing that his mind had been trained at the same time that he had gathered in a certain number of facts.

There was another feature of the university which we sometimes find it difficult to realize: the spirit of inquiry was rife among them. At that time the ways of thinking were devious; but still within the limited circle in which they moved, along the only lines then open to them, the thinkers used their minds in the spirit of free inquiry. When one reflects upon the circumstances in which they worked, one cannot help realizing that their long-drawn-out discussions were at bottom an expression of the love of inquiry, and that if they had had the advantages which we enjoy now, that which we call their subtlety would have broken out into discovery and invention.

Lastly, it was a feature of the university at that time that it was willing to take into its bosom any one who showed that he had any promise of benefiting by the instruction there given. It was an open home for all who wished for learning.

These are some of the features of the University of Cambridge in the olden times, and may we not, using them as a text, attempt to draw some conclusions as to what are the proper and essential functions of a university and what ought to be some of its guiding principles? As I said just now, the knowledge which they possessed was extremely limited, the facts with which they had to deal were very few. What can we say of knowledge at the present time? May we not say, if theirs was too little for them, ours threatens to be too great for us; that we are entering upon an age in which the facts which have to be learned and the various kinds of knowledge which have to be acquired are becoming too many for us? It is or it may be perfectly true that one of the advantages of learning is that it enables the learner to learn more rapidly; but is not this true, notwithstanding that the increment of knowledge is increasing far more rapidly than the increment of the power to learn? Is it not a serious matter for consideration that the things that the university has to teach are rapidly becoming far too numerous for the learner to learn? Is it not true that we cannot do now as they did in those old times, teach the student all that was known? We are compelled to make a choice, we must teach to the student some things and omit to teach him others. That is a necessity which it seems to me is increasing as the years go on. Nevertheless that position is a cruel one; for it may be truly said that every kind of knowledge has a value of its own; each kind of knowledge has for the learner a value which can be given by no other kind, and he who fails to gain any one kind of knowledge is thereby a loser. For building up the student into the full and complete man, the best course would be to take in all the knowledge which can be offered by a university; but as I said just now, a choice must be made, and the consideration of the principles which should guide the decision as to what should be chosen and what should be left demands the most serious attention. Here I think we may venture to follow the example of the old university. Admitting that each kind of knowledge is particularly fitting for a particular calling, that for every particular calling in life there is a knowledge, or there are kinds of knowledge which are suited or fitted for that calling and without which that calling can not be pursued with success, in the necessary choice which must be made between this study and that is it not a wise course to take that which best serves the future calling of the student? I cannot but think that in this choice of which I am speaking, the arguments for what are sometimes called technical education are unanswerable; that one of the principles of most importance in determining the choice of the studies to be taken up by the student lies in the fitness of the study for giving him power in the calling which he proposes to adopt. We must, however, remember that the knowledge which is thus to be imparted to him must be not merely a knowledge of facts, but bring with it the power of thinking. If technical education is understood in this way, not as a mere accumulation of facts, not as the mere heaping up of knowledge, but as the training of the mind in some particular kind of knowledge, the dangers, I venture to say, which some fear, will prove unreal, and it will be seen to be a true principle of university education.

There is another aspect in which we may look at university duties. May we not say that the tendency of modern civilization is to smooth down individual differences, and that the whole tendency of the environment of man is to make each

man increasingly more like his brother? There was a time when one could tell by the dress where a man came from, but this has become less and less easy, and it is not in dress alone, but in his very nature that man all over the world becomes more like his fellows. I myself during the short time I have been in this country have felt it more and more difficult to tell what are the differences between an American and an Englishman, and I trust that these differences are equally difficult to you. This may be a favorable aspect, but there is an unfavorable side to this continual influence of things about us. Mr. Francis Galton has shown that there is a great tendency in things to make men more and more alike in stature, and there seems a corresponding tendency to make men all alike in the stature of their minds. We seem tending in many ways to a monotonous mediocrity of intellect. This influence is especially strong among young people. I see for myself in the University of Cambridge that when one young man does one thing they all do it; they go astray like sheep, and they also go straight like sheep. Surely it ought to be a function of the university to counteract this tendency and so to bring the influences of learning upon the young as to develop individual differences. That I take it is one of the most important functions which a university can exercise, but one which is not always kept in view in university enactments. Here I can speak of my own university, and in doing so can lay the blame for the present condition of things on the traditions of the past. I find in my own university discouragement for the development of individual power. Every lad who comes to the University of Cambridge is compelled to pass through the same examination, to know the same things to the same extent, whatever may be the nature of his mind. He must know a little Latin, a little Greek, a little mathematics, a little history and one or two other subjects. Each one who comes, whatever his previous history, must pass through this one gate; the whole university has been pushed through this one common gate. Now I know that this may be defended; it may be said for instance that it is a bad thing not to know Latin. I quite agree with that. I think it a very bad thing not to know Latin, but I also think it a very bad thing for a lad to be thrown into life, it may be to go through life, without any clear idea whatever of the fundamental laws which govern the phenomena of living things. It may be said that it is a bad thing not to know Greek; I agree with that. Not to know Greek is to my mind worse than not to know Latin, but I think also that it is a bad thing for a lad to go through life ignorant of the fundamental laws of chemical action. If you go along in that line of argument you end by compelling a lad to know everything before he enters the university. If I had my way and could wipe out the traditions of the past I should vary that entrance examination. I should hold on to the old tradition of the university that it was ready to receive everybody who was likely to profit by its instructions. I should make the examination look, not backward as it does now, but forward, and should only insist that the lad must give such proofs of intelligence and industry as to lead to the hope that the years of university life would not be spent in vain. When the lad has really entered the university (at times he does not do so until he has spent two or even three years at the place in preparation, and sometimes goes away from the place without having really been admitted), it seems to me there should be a still wider scope for his studies. He has even now, it is true, an opportunity to take a degree in one or other of several branches of learning, but in each case he must follow out a particular schedule which has been laid down and which compels him to walk along a particular path and no other. If he wishes, for example, to study mathematics with philosophy, he would find that he could not do so, for in the examinations mathematicians have nothing to do with philosophy, and philosophy nothing to do with mathematics; and so in other things. I venture to think that this is not a satisfactory condition of things, and that throughout the whole academic course there should be a freedom of the young mind to develop in the line in which it was intended to develop. When I urge this upon my friends they all say, "It is very good, but it is impossible, the examination machinery would become so complicated as to break down." But I would ask the question, Are examinations all in all? were the examinations made for universities, or were universities made for examinations? I myself have no doubt about the answer. I trust that this new university, which can walk with freedom along new lines, will find some way of so arranging studies and examinations that the two will not conflict, and that anybody coming here will find that the particular gifts that have been given to him and which it was intended should be developed will meet their fullest expansion.

Lastly, there was another feature which the old university possessed and which I may also call an essential feature of a university, that is, the spirit of inquiry. No university can prosper as a university that not only does its best to favor special inquiries when these are started within it, but also in the whole course of its teaching develops, or strives to develop the spirit of inquiry. Now here again I fear that examinations—such at all events is my experience—are antagonistic to inquiry; and I would suggest that in arranging examinations one ought always to look ahead to see how far one can possibly order those examinations so as to favor the teaching which teaches in the real and true way, teaching by regarding each bit of learning as in itself an act of inquiry, and so as to favor in the highest degree actual inquiry when it is taken in hand. This of course is antagonistic to one function of examinations, namely, that of putting young men to compete against each other. You cannot so judge inquiries as to put the inquirers in any class list or in any order; the most you can do is to give an inquiry the stamp of approval of the university, a testimony that the inquiry has been carried out in a satisfactory way. It is true that in this way you lose that which is sometimes thought to be of great value, emulation between the scholars; but if you take away that kind of emulation you substitute for it another one far more strong and effective, that emulation that comes of striving with nature. I take it that the good which is done to a lad in starting him upon an inquiry is infinitely greater than any which can be gained by competition with his fellow students. Here I am glad to say a good word for my own university; for we have in a very quiet way, and unobserved, secured the adoption of an enactment which allows a lad to enter the

university and obtain his degree and all which follows upon that without entering into a single examination. At the present moment it is possible for one, it is true under exceptional circumstances, to come to the University of Cambridge in England, and if he convinces a competent body of judges that he is a person likely to carry on inquiry in a successful manner he can enter the university as a student, and if he satisfies another body of men after a time that his inquiries have resulted in a real contribution to knowledge he can secure his degree. He can get that without ever having touched a written examination paper, and I am proud that we are able to offer that to the world; for it has happened again and again that a man who had real genius for a particular line of inquiry stumbled over the preliminary studies of which I have spoken, knocked at the door of our university in vain and was sent way. Now such an one would be admitted, and I venture to say that in the long run the university will be the gainer.

These then are some few thoughts concerning universities and their methods. I say I have purposely learned nothing about your enactments, but from what I know of your short past I feel confident that this university will in the future be conspicuous for progress. May I hope that it will carry on education along some of the lines which I have indicated to-day, and perhaps some day we in the old country may mend our ways after your pattern.

THE RESULTS OF THE INTRA-TRACHEAL INOCULATION OF THE BACILLUS DIPHTHERIÆ IN RABBITS.

By Simon Flexner, M. D., *Baltimore*, and H. B. Anderson, M. D., *Toronto*.

[*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*]

I.

The interest which was aroused by the discovery of Frosch,[1] Kolisko and Paltauf,[2] Wright,[3] and others, that the bacillus diphtheriæ not uncommonly invades the internal organs in diphtheria, was further stimulated by the publication of the work of Kutscher, which dealt with the relation of the bacillus diphtheriæ to the pneumonic processes that are associated not infrequently with pharyngeal and laryngeal diphtheria. The studies of the foregoing writers, which will be examined more in detail hereafter, led to the supposition that, contrary to the previously expressed views concerning the ætiology of the pneumonic processes in diphtheria, it was probable that in many cases the diphtheria bacillus might itself be the causative agent. In the winter of 1894 we presented to the Johns Hopkins Hospital Medical Society a preliminary communication on the subject of the effects of the injection of pure cultures of the bacillus diphtheriæ into the tracheæ of rabbits. We were then able to say that by this means a definite and wide-spread pneumonic process could be provoked, which led in many instances to the death of the animal. These experiments seemed therefore to be more conclusive than the previous observations upon human beings with reference to the probable action of the diphtheria germ in this respect, for the reason that in the former subsidiary or secondary micro-organisms were definitely excluded from any part in the production of the pathological lesions. Our studies carried us incidentally into a consideration of the fate of the introduced micro-organisms, as it soon appeared that even after considerable numbers of diphtheria bacilli in pure culture had been inserted through the trachea into the lung, their recovery from these situations was often attended with much difficulty and sometimes was impossible.

Although the credit of the demonstration of the invasion of the internal organs by the bacillus diphtheriæ has usually been given to Frosch, it is an undoubted fact that Loeffler[4] had previously encountered these organisms certainly in the lungs and perhaps in the liver, in human beings. In the light of our present knowledge it is interesting to note how Loeffler endeavored to explain away these observations on the supposition that the bacilli had entered these organs post mortem and not during life.

In briefly reviewing the literature we shall confine ourselves to a consideration of those instances in which the organisms have been isolated either alone or together with other bacteria from the lungs, more particularly in association with pneumonic processes.

In the communication in which Frosch[1] pointed out the common invasion of the internal organs by the specific bacillus in cases of diphtheria he states that the organisms were present in the lungs and elsewhere. Without giving any particular details, he adds that as compared with the remaining viscera they were found most often in pneumonic areas, the spleen and the lymphatic glands. Whether they existed there alone or in association with other micro-organisms he does not say. One is led to believe, however, that in a majority of instances at least other micro-organisms were present, inasmuch as he states in conclusion that in almost all of his cases he found a mixed infection with various kinds of bacteria, but generally with streptococci and staphylococci.

Kutscher[5] investigated the invasion of diphtheria bacilli into the lungs in human beings and their relation to the broncho-pneumonias of diphtheria. For this purpose he studied the lungs of ten children who came to autopsy, and in whom the diagnosis of diphtheria had been made during life. Cultures were made in a part only of the cases; sections of the organs, however, were studied in all. The cases included examples of pharyngeal and laryngeal diphtheria with extension into the bronchi. The results arrived at by Kutscher indicated that in a small number of instances the

bacillus diphtheriæ may be contained alone within the consolidated patches in the lungs, but that there is likely to be an association of bacteria, the chief accompanying forms being the pyogenic streptococci and staphylococci. Diphtheria bacilli were absent from the lung tissue not the seat of hepatization; not so, however, the streptococci. In some instances the consolidation was entirely microscopic, and in these cases streptococci were found without lesions being present about them, while, on the other hand, the diphtheria bacilli were discovered only in the broncho-pneumonic foci.

As a result of these studies Kutscher[8] expressed himself to the effect that the lungs must be considered as the organs most often and most severely implicated in the secondary invasion of the diphtheria organisms. He regards the commonest mode of invasion to be by aspiration, which certainly must be the most usual way, and places next in order of frequency an infection through the lymphatic channels on the ground that bacilli were found in the perivascular lymphatics. Kutscher further pointed out that in not a single instance was he able to demonstrate the presence of these micro-organisms within the blood-vessels themselves. The question whether the bacilli in the internal organs may themselves be the cause of lesions he believes must be answered affirmatively with reference to the lungs. In support of this belief he urges that the bacilli have been found not only in advanced lesions, but often and alone in the earlier ones, and that they occur in bronchi which are little affected, as well as in those filled with a cellular exudate in which the epithelium has been largely destroyed. The probability of the bacilli being secondary invaders after the pulmonary lesions had been brought about in other ways is therefore excluded.

Although in a few cases diptheria bacilli had been demonstrated in the lung by Johnston,[9] Strelitz,[9] Booker[10] and one of us (Flexner[11]), the next series of examinations comprising a larger number of cases, and therefore of more conclusive significance, was furnished by Wright, who, in studying fourteen fatal cases of diphtheria, isolated this organism from the lungs in thirteen. For the most part there existed broncho-pneumonic areas in which these bacilli were found, although they were associated, as a rule, with the usual pyogenic cocci. In ten of the fourteen autopsies there were distinct lesions of broncho-pneumonia, but the occurrence of the Klebs-Loeffler bacillus in the lung seemed to be independent of the coincidence of these lesions, for, as Wright points out, it was absent in at least one instance of broncho-pneumonia, and present in the tissues in the absence of these lesions. The diphtheria bacillus was associated with the streptococcus in nine cases, in seven of which pneumonia was present.

In a subsequent report by Wright, associated with Stokes,[4] an analysis of thirty-one cases of diphtheria is given, in which cultures from the lungs revealed the presence of the Klebs-Loeffler bacillus alone or in combination in thirty out of the thirty-one cases examined. Of these thirty-one cases broncho-pneumonia was present in nineteen.

Their series of cases also shows that the diphtheria bacillus may be present in the lungs independently of the occurrence of broncho-pneumonia, for in twelve cases in which no pneumonic condition was demonstrable, cultures from the lungs showed the presence of these micro-organisms.

Belfanti studied a series of 26 cases of broncho-pneumonia associated with diphtheria and found the Klebs-Loeffler bacillus in 21. Of these 21 cases it was present alone in four, and combined with other bacteria seventeen times.

The most recent contribution to this subject has been furnished by Kanthack and Stephens,[12] who report that of twenty-six fatal cases in which the lungs were examined for their presence, the Klebs-Loeffler bacilli were found in every one with ease and in large numbers. In comparing these results with those obtained from a similar examination of other organs of the body, these authors conclude, and on this point agree with Frosch and with Wright, that the Klebs-Loeffler bacillus escapes most readily into the lungs; indeed they urge that in these organs the bacilli are found not in small numbers, as had been previously considered, but are very numerous. Of the twenty-six cases examined, Kanthack and Stephens describe the lesions of broncho-pneumonia in fifteen, and state that they must take exception to the statement frequently made that the broncho-pneumonia in diphtheria is of pyococcal origin, maintaining that it would rather appear to be a veritable diphtheritic complication. It is worth mentioning that the broncho-pneumonias of diphtheria are according to them most frequently encountered in those cases in which the invasion of the larynx by the membrane had taken place. Of twenty-four laryngeal cases which they describe, broncho-pneumonia existed in thirteen.

In interpreting the results of the observations upon the relation of the pyogenic organisms to broncho-pneumonic areas in the lungs with or without the coincidence of the Klebs-Loeffler bacillus, we must take exception to the statement made by Kanthack and Stevens[13] that "staphylococci, pneumococci and streptococci are normal inhabitants of the bronchi, bronchioles and alveoli; and therefore on cultivation must of necessity appear on the agar-agar surfaces." We think a sufficient answer to this statement is found in the frequency with which such cultures from perfectly normal human lungs at autopsy give negative results. We are far more inclined to regard the pyogenic organisms as not without pathological significance, notwithstanding the fact, as we hope to show, that the diphtheria bacillus is quite capable alone of causing definite pneumonic processes.

II.

The results derived from our studies of the intra-tracheal inoculation of fluid cultures and suspensions of the Klebs-Loeffler bacillus were unmistakable in their significance. We were able in quite a number of cases to provoke an inflammatory process within the lungs which varied in extent, involving sometimes a small area, even a fragment of the lobe, and at others the greater portion of one lung, or considerable parts of both. In the course of these studies attention was directed to some other points, more or less in dispute, and especially to the question of the fate of the introduced micro-organisms and the length of time during which they were demonstrable within the substance of the lungs.

The method pursued in conducting these investigations was

quite simple, and after a few preliminary failures uniformly successful. It consisted of exposing the trachea above the clavicles in half and full-grown rabbits, the precaution having first been taken of carefully removing the hair over the site of operation. The only real difficulty which was encountered was the avoidance of infection of the tissues about the trachea. In the early experiments this was not always successfully overcome, but later, by introducing the needle through a small pledget of sterilized cotton, placed in contact with the exposed trachea, and withdrawing it through the pad, we were able as a rule to avoid infection of the soft tissues. The wound was sutured and covered with a celloidin dressing.

The amount and the character of the injected material varied with the different cases and are recorded in the individual protocols. The duration of life succeeding inoculation also varied considerably, and the extent of lung involvement seemed to depend more or less upon the period of incubation. For the study of the pneumonic process in its entirety inoculated animals were allowed to live as long as possible, while for the study of the fate of the introduced micro-organisms, as well as the time required for the development of the pathological lesions, the animals were killed at intervals varying from one to twelve hours after inoculation.

Our attention was attracted in the early experiments to the frequency with which, in the hepatized lungs, the introduced bacilli were missed in cultures, in cover-slip preparations, and in the tissues, so that it became necessary to search elsewhere for them, or to discover the manner of their destruction *in situ*.

Exp. 1. Full-grown white rabbit received Feb. 10, 1895, .5 cc. of a bouillon culture of the bacillus diphtheriæ reinforced by the addition of five drops of the condensation water of a serum culture two days old. It lived about 65 hours.

Autopsy. Practically no reaction about the local wound; the lymph glands neither enlarged nor congested. The mucous membrane of the trachea near the larynx showed a few small points of congestion. The trachea and bronchi contained frothy serum. The lungs were voluminous and completely consolidated excepting the edges of the lower lobes, which contained air. The pleural surfaces showed points of ecchymosis and had a moist, somewhat glutinous appearance. The consolidated portions presented a peculiar semi-translucent gelatinous appearance, and on section an œdematous fluid in small quantities escaped. The remaining organs showed nothing remarkable.

Bacteriological examination. Trachea; no diphtheria bacilli found. Pleuræ; no bacilli found. Lungs; films were examined from various portions, and no distinct bacilli could be found. What may have been pale and perhaps degenerated organisms, two or three in number, were found on one cover-slip. Many pus cells containing amphophilic granules were present.

Cultures on Loeffler's blood serum from the consolidated portion of the lungs, the heart's blood and liver were perfectly negative.

Exp. 2. Full-grown Maltese rabbit received .5 cc. of a 48-hour old bouillon culture on Feb. 7th. Death in 47 hours. Autopsy immediately after death. Heart still beating slightly, but irregularly. Trachea filled with frothy serum. The lungs, with the exception of the edges of the bases and apices, which contained air, completely consolidated. They were voluminous and completely filled the pleural cavities. Beneath the pleura were small hæmorrhagic points. Upon section the smooth gelatinous appearance described in the previous animal was observed. The trachea showed slight congestion at the point of entrance of the needle.

Bacterioscopic examination. In the trachea in the neighborhood of the puncture a few diphtheria bacilli were found, both free and enclosed in epithelial cells. Examination of the pleura was negative. In the lungs what may have been a few extracellular degenerated forms.

Cultures from the lungs and heart's blood negative.

Exp. 3. Half-grown rabbit received .5 cc. of a slightly turbid suspension in condensation water of a blood-serum culture. Died in 27 hours.

Autopsy. The trachea much congested throughout and covered with punctiform hæmorrhages, but without visible membrane. The œsophagus also much congested. The local wound somewhat swollen and œdematous. The superior lobes of the right lung were almost completely consolidated, the remainder contained air.

Bacterioscopic examination. From the exudate about the trachea a small number of diphtheria bacilli. From the lungs and pleura, negative; from the œsophagus, typical bacilli.

Cultures. Heart's blood and lungs on Loeffler's blood serum negative.

Exp. 4. A white half-grown rabbit received .5 cc. of a bouillon culture reinforced by the addition of five drops of the condensation water of a serum culture two days old. The animal succumbed on the seventh day. There was absolutely no pneumonia; the lungs appearing somewhat congested, but contained air in all parts.

The cultures were negative. Cause of death not apparent.

Exp. 5. Full-grown rabbit received at 3.15 P. M., June 22nd, .9 cc. of a turbid suspension. Died during the night.

Autopsy. Trachea, no membrane; somewhat congested.

The lungs much congested; no definite consolidation.

Bacterioscopic examination. From trachea numerous bacilli, both free and within cells.

Lungs. Upon cover-slips many polymorphonuclear cells, but no bacilli.

The cultures showed Klebs-Loeffler bacilli in the congested portion of the lungs, the bone-marrow (femur) and the heart's blood.

This series of cases shows in the first place that the diphtheria bacillus by itself is capable of provoking a definite and often wide-spread pneumonic process when introduced directly into the lungs of rabbits; but that in certain cases, notwithstanding the entrance of numerous bacilli into the lungs, a pneumonic process fails to be provoked. Further, it shows that when the number of bacilli is great the animal may succumb, presumably to the intoxication induced by these organisms, before an outspoken pneumonia has developed, thus illustrating anew the effects of the absorption of the poisonous products from the lung substance. Again, Experiment 5 shows that in addition to the invasion of the body presumably by the toxic products of the diphtheria bacillus, we may have a more or less wide distribution of the organisms themselves, and that they may be found in very distant situations. Finally, this series of experiments proves that after the provocation of the pneumonic process the bacilli may themselves either disappear completely, or be so reduced in numbers as to be incapable of demonstration in cover-slips, or that their vitality may be either destroyed or interfered with to such an extent that any attempt at cultivation, even on favorable media, will be followed by negative results.

Exp. 6. A full-grown rabbit received 1.3 cc. of a turbid suspension in bouillon of the bacillus diphtheriæ. The animal was killed by a sharp blow on the back of the neck one hour after the inoculation.

Autopsy. The lungs were voluminous and slightly mottled. Hæmorrhages were not discovered beneath the serous membrane.

Bacterioscopic examination. Cover-slips from the lower lobes of the lungs showed, besides a few polymorphonuclear leucocytes containing amphophilic granules, and some few epithelial cells, bacilli singly as well as in small and in large clumps, chiefly existing free among the cells. Occasionally enclosed within an epithelial cell there was to be found a single bacillus, and more rarely several bacilli. The cells which contained the bacilli stained in the same normal manner as the remaining cells, and the bacilli themselves showed no variation in staining properties as compared with the extracellular forms.

Cultures. From both apices and bases of the lungs a variable number of colonies of the introduced bacilli; from the pleural membrane a single colony of the same organism. The heart's blood, spleen and bone-marrow gave negative results.

EXP. 7. A black, nearly grown rabbit received 1.3 cc. of a turbid suspension similar to the last; the animal was chloroformed after the lapse of one hour.

Autopsy. The lower lobes of both lungs were swollen, slightly congested, and the serous membrane covering the lungs showed here and there punctiform ecchymotic spots.

Bacterioscopic examination. The cover-slip preparations from the various parts of the lungs showed essentially the same appearances as those described for the previous experiment, but it seemed as though the cells containing bacilli were perhaps a little more numerous in this case. The polymorphonuclear amphophiles appeared to be about as numerous as in the preceding experiment, and as in that case the introduced bacilli were never found within these cells. An examination of the bronchial epithelium showed a complete absence of bacilli within the columnar epithelial cells, even when they were quite numerous between them.

Cultures. From the lungs, considerable growth of the introduced bacilli. From the heart's blood, bone-marrow and spleen the cultures remained sterile.

EXP. 8. A nearly full-grown rabbit received on Feb. 26th 1 cc. of a turbid suspension of the bacillus diphtheriæ. The animal was killed at the end of 3½ hours.

Autopsy. Lungs voluminous. In the superior and inferior lobes of both lungs considerable hæmorrhages existed beneath the pleura, which on section could be seen to extend into the lung substance. Admixed with the blood there was much frothy serum; elsewhere the lung tissue was pale and moderately dry.

Bacterioscopic examination. Films prepared from the hæmorrhagic areas showed large numbers of epithelial cells enclosing diphtheria bacilli. The bacilli were often arranged in the same parallel rows which one observes in the cover-slip preparations from the cultures themselves. The bacilli stained in all respects normally; rarely there appeared within the cells specks of chromatin which had the same staining property as the bacilli and might have been fragments of the latter, but they were hardly more numerous than one occasionally finds in cultures of the same organism. The cells containing these bacilli themselves appeared entirely normal. The bacilli were very rarely found to have invaded the nuclei of the cells. Leucocytes with typically polymorphous nuclei were present in the cover slips, but they were never seen to contain the inoculated bacteria. The free bacilli were seen only exceptionally among the cells; when found here they were usually single and rarely in clumps.

Cultures. The lungs and spleen gave growths of the bacillus diphtheriæ. From the heart's blood the cultures were sterile.

EXP. 9. Nearly full-grown rabbit received .5 cc. of a faintly turbid suspension of the bacillus diphtheriæ. Killed after six hours.

Autopsy. Lungs partly collapsed; the pleura covered with small hæmorrhages. The lower lobes of the lungs were congested and œdematous; no definite consolidation.

Bacterioscopic examination. The films from the superior and middle lobes were negative. From the congested and œdematous lower lobes bacilli in small numbers were obtained, occurring singly and in small groups, extracellular and enclosed within epithelial cells. The polymorphonuclear cells, which showed an increase in number as compared with the two previous cases, did not contain the introduced micro-organisms.

Cultures from the lungs and spleen were positive; from the heart's blood no growth was obtained.

EXP. 10. Full-grown rabbit received .75 cc. of suspension of a culture on blood serum two days old. Animal killed at the end of six hours.

Autopsy. The trachea at the seat of inoculation showed some congestion but no false membrane. The bases of the lungs were congested, the pleura covered with minute hæmorrhages.

Bacterioscopic examination. (a) Smears from the mucous membrane of the trachea at the site of inoculation showed diphtheria bacilli in considerable numbers, all extracellular, and among these polymorphonuclear cells. (b) From the base of the lungs mononuclear, epithelial and polymorphonuclear cells, the former containing bacilli. Similar micro-organisms, although in smaller number, also existed between the cells.

Cultures. From the lung a large number of colonies. From the spleen, bone-marrow, heart's blood and liver, smaller numbers of colonies of the introduced micro-organisms.

EXP. 11. A rabbit received .75 cc. of a turbid suspension of a growth of the bacilli upon blood serum. Killed at the end of twelve hours.

Autopsy. Trachea about the site of inoculation showed much congestion, which extended above and below the point at which the needle had been introduced, but no false membrane existed. The caudal lobes of the lungs were much congested, and beneath the pleura minute hæmorrhages appeared. The spleen appeared enlarged.

Bacterioscopic examination. Smears from the trachea showed numerous polymorphonuclear cells, but no bacilli. From the lungs (bases) bacilli extracellular and polymorphonuclear cells.

Cultures. From the heart's blood, spleen and bone-marrow the introduced bacilli were cultivated. From the tracheal glands and lungs the tubes were negative.

EXP. 12. Was a repetition of the previous experiment and gave similar results, with the exception that the bacilli were cultivated from the congested and œdematous lower lobes of the lungs. It is therefore probable that in the previous case the absence of the bacilli from similar situations is to be regarded as an accidental occurrence.

EXP. 13. Full-grown rabbit received .80 cc. of a suspension of the bacillus diphtheriæ. Killed in 18 hours.

Autopsy. The trachea appeared very much congested, but there was an entire absence of false membrane. The caudal lobe of the lung on the right side was dark red in color, but not frankly consolidated, whereas on the left side a definite consolidation in the corresponding lobe had taken place. The spleen was decidedly enlarged and congested.

Bacterioscopic examination. Cover-slips from the trachea showed many polymorphonuclear cells, fewer epithelial cells, no bacilli. From the lungs many polymorphonuclear cells and epithelial cells with single nuclei, but no bacilli.

Cultures from the lungs and heart's blood, positive; from the spleen, liver and bone-marrow, negative.

EXP. 14. A large rabbit received 1 cc. of a bouillon culture. Killed after 24 hours by breaking up the medulla.

Autopsy. The middle lobe of the right lung contained a consolidated patch the size of a silver dollar, over which the pleura was congested and contained small hæmorrhages.

Bacterioscopic examination. Films from the consolidated portion of the lung showed many polymorphonuclear leucocytes, some epithelial cells, but no bacilli.

Cultures from the lung as well as heart's blood, spleen and bone-marrow were negative.

Exp. 15. Full-grown rabbit received .75 cc. of a turbid suspension derived from a blood-serum culture. Killed in 24 hours.

Autopsy. The caudal lobe of the right lung and the lower part of the cephalic lobe on the same side were congested and consolidated as well. In addition the caudal lobe of the left lung contained several smaller areas of consolidation. The spleen was much enlarged. The trachea over the site of inoculation and at a distance from it was much congested. There was an entire absence of false membrane.

Bacterioscopic examination. Smears from the consolidated portions of the lung, trachea, spleen, bone-marrow and heart's blood were all negative.

Cultures from the same sources remained entirely sterile.

The object of this group of experiments was two-fold, namely, to determine, if possible, the manner in which the introduced bacilli so completely disappeared, and in the next place to consider the length of time necessary for the development of the pneumonic processes and the nature of the inflammation provoked.

Animals which had received large numbers of the Klebs-Loeffler bacilli showed at the end of one hour changes in the lungs, which, however, were not very marked. They consisted simply of an œdema of the tissues, together with more or less mottled congestion. Of greater significance, however, was the fact that an emigration of leucocytes had already taken place, and that some, although few, of the introduced bacilli were enclosed within cells, these being exclusively the epithelial cells of the alveoli. At the end of 3½ hours the pathological process was much more advanced, the first expression apparently resulting from changes in the blood-vessels, to judge from the definite hæmorrhages, often of considerable extent and very numerous, which were discoverable both in the pleura and in the substance of the lung. By this time, although large numbers of the bacilli had been introduced, comparatively few were now free, the overwhelming majority of them being enclosed either within the protoplasm or the nuclei of cells. In this short time the bacilli might be found to have extended their invasion beyond the thoracic organs; and whereas at the end of one hour they were still limited to the substance of the lungs, at the end of 3½ hours they were found in the spleen as well. It should be mentioned here that owing to the small size of the bronchial lymphatic glands, cultures from these were not very satisfactory, and were therefore not regularly made. At the end of 6 hours the effects of the inoculation were still more noticeable, and the distribution of the micro-organisms more extensive, as they were demonstrated by the culture method at the end of this time in the heart's blood, spleen, bone-marrow and liver. The bacilli were still capable of cultivation from these distant organs as well as from the lungs at the end of twelve and eighteen hours, while after the lapse of twenty-four hours, at which time a frank consolidation of the lung substance had taken place, they could not be cultivated either from the lungs or from the remaining organs mentioned. We should like to emphasize that, although the inclusion of the bacteria by cells takes place so rapidly and extensively, in no instance did we succeed in discovering the bacilli within the substance of the polymorphonuclear leucocytes.

The foregoing experiments serve to confirm the observation upon human beings relating to the existence of a purely diphtheritic broncho-pneumonia, and lend support to the view that the laryngeal cases are specially prone to the development of such pathological conditions, as they present the most favorable opportunity for the direct aspiration of the infectious agent. That an actual increase of the introduced micro-organisms takes place is proven, we think, by the observations made upon human beings which have been given in detail in an earlier part of this paper; in view of which fact the disappearance of the introduced bacteria in cases of experimental inoculation is all the more perplexing. The interpretation of this phenomenon is indeed not at once apparent. On the other hand it is worth considering whether in those cases of human diphtheria in which the bacilli have not been found in the local pathological processes, it may not be also unjustifiable to conclude that the bacilli never were present there, and were not concerned in their causation.

It is certainly interesting to observe that there may take place from the lungs a rapid distribution of the introduced bacilli throughout the body, so that at the end of from four to six hours they may be found widely distributed throughout the organs. It has appeared to us as if the opportunities for such distribution are greater in cases of intra-tracheal inoculation than in the ordinary modes of subcutaneous inoculation, where, as is well known, the bacilli are not found extensively distributed through the viscera. However, there is at least one difference between the observations in the two sets of cases, for in the course of the ordinary subcutaneous inoculation a longer time as a rule elapses between the inoculation and the death of the animal, which may account for the absence of the bacilli in the internal organs. As an illustration of this point we may mention that in animals which were either killed after the lapse of twenty-four hours or died spontaneously later, we failed to obtain the introduced bacilli from these viscera.

The experiments which we have conducted justify us in considering for a moment the question of the action of the lungs as an infection atrium into the body of pathogenic micro-organisms, and they would lead us to agree with Hildebrandt,[12] who showed, contrary to the previous belief of Flügge,[14] that the alveolar epithelium is not a perfect barrier to the invasion of pathogenic bacteria from the interior of the lungs. At the time that the bacilli are already well distributed through the body the alveolar epithelium still appears entirely normal, although containing many bacilli within its substance. The supposition that bacilli are capable of passing from the bodies of the epithelial cells in some way into the general blood current or into the lymphatics, without leaving behind them obvious evidences of injury to these structures, would therefore appear to be justifiable. As to the mechanism of this procedure one can only deal in conjectures, when it is remembered that in this case we are dealing with non-motile organisms which must be transported from place to place by a force not resident within themselves.* The capacity of the alveolar epi-

*Ultimately, of course, this is the same problem as that dealing with the mode of passage of inert particles, such as soot, india ink

thelium to take up living foreign matter in the manner similar to what is observed in dust inhalation had been previously observed by Muskatblüth[15] in his experiments upon the effects of the intra-tracheal inoculation of anthrax spores. He observed that in animals which had been killed on an average sixteen hours after inoculation, the greater majority of the bacilli were contained within epithelial cells corresponding with the so-called "staubzellen." Even when the englobing cells were free in the alveoli they gave every indication of having been derived from the pre-existing epithelium of these parts, and indeed were often found to be still in connection with the latter. As in our observations, he found that the leucocytes, the phagocytes *par excellence*, had no part in the inclusion of the bacteria. He was neither able to detect evidence of injury to the cells containing the bacteria, nor that the bacteria within them were undergoing disintegration.

It must not be forgotten that after the introduction into the lungs of such numbers of bacteria as were inoculated into these animals a portion at least of them may have been thrown off through the bronchial secretions. In this way not an inconsiderable number may have been finally disposed of, and this possibility is rather strengthened by the observation of Case 3, in which an inflammation of the œsophagus was noted and the Klebs-Loeffler bacilli were found in considerable numbers in this situation. Muskatblüth regarded the reaction on the part of the lungs, with the pouring out of inflammatory products, as favoring the destruction of the anthrax organisms *in situ*, a conception which could, with more or less justice, be applied to the cases in which at autopsy in the pneumonic areas we failed to obtain the introduced micro-organisms. It is, however, probable in the light of our present knowledge of the mechanisms employed by the animal body to dispose of pathogenic and other micro-organisms, that no inconsiderable action must be attributed to the spleen, liver and bone-marrow.

It appears to be worth while to direct attention to the fact that in not one of our animals was a pseudo-membranous tracheitis observed, although evidences of inflammation were more or less common. This is probably to be explained by the assumption that the injury to the mucous membrane was too slight to afford a favorable opportunity for the development of the organisms in that situation, rather than that the animals did not live, or were not permitted to live, long enough for the membrane to develop.

III.

In order to study the development of the pathological lesions in the lungs, sections of these organs were studied in the following manner: Beginning with the lungs of the animals killed one hour after inoculation, the succeeding ones were examined in a consecutive series. Sections were prepared from different parts of the organs; in those in which consolidation was apparent the hepatized portions were always included. The staining agents employed consisted of hæmotoxylin and eosin, safranin in aqueous solution, and Weigert's fibrin stain. The last sufficed for staining the bacteria, as well as fibrin, when present or when capable of retaining the dye, which was by no means always the case.

The histological lesions in the animals killed after one hour were very inconsiderable and consisted of dilatation of the alveolar capillaries, extravasation of a few red blood corpuscles, the appearance of polymorphonuclear leucocytes in occasional alveoli and in the bronchial walls, more rarely in the lumina of the bronchi in small numbers, perhaps an increase in the flat epithelial, nucleated cells within the alveoli, and more or less œdema. At the end of three and a half hours, on the other hand, the pathological condition was well advanced. Small vessels, apparently arteries, contained fibrinous and leucocytic thrombi; the congestion of the alveolar capillaries and larger interlobular vessels was a striking feature; the blood within the vessels contained an increased number of white elements, and both red and white blood corpuscles had begun to leave the vessels in relatively large numbers. The alveoli contain many cells of an epithelial habitus, and the fact of desquamation of the alveolar epithelium is made directly apparent. There exists at this time a definite purulent bronchitis. Branches of the bronchial tree which are still lined with columnar ciliated epithelium contain many polymorphonuclear leucocytes, and similar cells may be discovered working their way through the walls of the bronchi to reach the lumina. The lining epithelium of these structures was never found to have suffered severely; no defects existed in this layer. A few cell fragments were seen amid the increasing cellular accumulations.

The animals which were permitted to live six hours showed much more advanced lesions. Up to this time the pathological changes have been limited to the interior of the bronchi and alveoli; but now the stroma of the lungs begins to show changes. As a whole it is thickened, partly owing to œdema and partly to an increase in the cellular constituents. Many of the new cells are polymorphonuclear leucocytes, but among these are many cells with round, solidly staining nuclei which may have been derived from such leucocytes or have had a different origin. Fragments of cells begin to be more common in this situation and karyokinesis begins to be apparent. The capillaries, chiefly those in the alveolar walls, show large, somewhat diffusely staining, nucleated protoplasmic masses resembling giant cells. That these masses are the results of the fusion of intravascular white elements seems highly probable. The endothelium of the capillaries and small veins is swollen, but no actual injury was observed. The number of cells within the alveoli is much increased; they still consist of polymorphonuclear and epithelial elements in about equal proportions. Definite mitotic figures begin to be fairly common within the alveolar epithelium, and an occasionally non-nucleated (necrotic?) cell of this kind makes its appearance.

and red blood corpuscles, through the alveoli. Arnold in particular has investigated this question and found that these substances are transported to and deposited within the neighboring lymphatic glands. Baumgarten[17] regards the transportation of bacteria and spores of fungi to be likewise of a purely mechanical nature. Moreover, he found that pathogenic bacteria were capable of being mechanically taken up in the same manner, in the absence of lesions of the alveolar lining; for the intra-tracheal injection of tubercle bacilli, killed by boiling, was followed by their passage in a few hours through the alveolar walls into the intra-pulmonary lymph follicles.

The bronchi contain much exudate, consisting chiefly of leucocytes with irregular nuclei, but mononuclear epithelial cells are also present, and a large amount of detritus derived by fragmentation from cell nuclei. Evidence of cell destruction to a slight extent is to be observed in the walls of the bronchi, and it not infrequently extends into and involves the lymph nodes imbedded in their walls. The lining epithelium shows little or no injury. As regards the origin of the cells composing the exudate within the bronchi it may be said that the bronchial mucous membrane furnishes but few of the elements. They come almost exclusively from below, from the terminal bronchioles in which the lining epithelium is almost or quite flat, and from the adjacent atria and air-sacs (Miller).[16] Specimens twelve hours old show still more clearly that the contents of the larger bronchi are excreted from below, inasmuch as the terminal structures give every evidence of a rapid filling up with cells, while the high epithelium of the former is quite perfect and the bronchial walls but little infiltrated with wandering cells. It is not alone the lumina of the bronchioles, the atria and the air-sacs which give evidences of increased cellular invasion; this is also apparent in the stroma as well. The much thickened stroma is overloaded with cells, having as a rule irregular and fragmented nuclei, and showing in addition, here and there, karyokinetic figures, some of which certainly would appear to be within the capillaries. Moreover, the air-cells springing from all these structures, terminal bronchioles, atria and air-sacs, are now more or less completely filled with cells, partly emigrated, partly desquamated from the walls. Fibrin is present in the form of fine fibrils, too fine apparently to retain the Weigert stain, but yet evident upon close inspection. The consolidation of the lungs at this early stage is partial only, and more microscopic than macroscopic in form. Œdematous foci and small areas of extravasated blood are intermingled. The pleura is still intact. The succeeding stages, that is, after 24, 47 and 65 hours, show appearances similar to those described, with such modifications only as involvement of larger areas and more perfect solidification might be expected to introduce. Adjacent to hepatized foci others of compensatory emphysema or insufflation exist, and the cellular infiltration of the stroma, always a prominent feature after twelve hours, may involve the emphysematous parts. Hæmorrhages are never entirely absent and may become considerable in the cases of longer duration; fibrin, never a very prominent feature, increases more or less;* multiplication of cells resembling the offspring of epithelial cells may be so rapid as in some places to be the sole elements within certain alveoli; the pleura becomes the seat of small leucocytic accumulations upon its surface which are derived from the lung substance, the cells of which may be seen wandering through the endothelial layer, which itself remains intact. Fibrin was never discovered upon its surface. The extent of destruction of nuclei within the bronchial as well as in the alveolar exudates grows until in many places fragmented nuclei alone compose the consolidating material. In this respect the exudate differs from most of those with which we are familiar in the lungs in acute disease. Even where a whole lobe, or indeed a whole lung, apparently is hepatized, the consolidation is not complete; the effect is brought about by the imperfect approximation of many foci of lobular consolidation.

The experimental pneumonias following the intra-tracheal inoculation of pure cultures of the bacillus diphtheriæ in rabbits are lobular or pseudo-lobar in character; they are cellular pneumonias for the most part, fibrin playing a relatively inconsiderable rôle in their production; they are rapidly developed and originate in the bronchioles, atria and air-sacs; the bronchi are but little affected in the early stages, and even later are hardly more involved than in the acute lobar pneumonias of human beings. The bacillus diphtheriæ and its toxic products when introduced directly into the lungs exert their action primarily upon the blood-vessels; very soon, however, the alveoli themselves are deleteriously affected, and within the brief period of six hours the entire framework of the lungs feels the injurious influence. The expression of these effects is seen partly in the exudative and partly in the proliferative changes which ensue. Among the latter the appearance of cell division by mitosis after the lapse of only twelve hours seems worthy of special mention.

The relation of the bacilli to the lung structures is a simple one. Sections stained in Weigert's fibrin stain show, in those cases in which the duration of life of the animal did not exceed twelve hours, many of the characteristic bacilli. They were almost never free, but enclosed in cells, which were either distinctly mononuclear in character or large, flat and scale-like, without demonstrable nuclei, and certainly not of the nature of vascular leucocytes. That they have come from the alveoli is certain, for similar cells crowded with bacilli may at times be found still attached to the walls. The study of the relation subsisting between the micro-organisms and the lungs shows conclusively that the invasion takes place from the bronchioles, and very soon the bacilli are discovered within cells in the stroma. Whether or not they were contained within definite vessels could not be determined with certainty.*

Within the bronchi the bacteria appear amid the cellular exudate sometimes enclosed within the scale-like cells mentioned, and again, but not certainly, within polymorphonuclear leucocytes. If actually englobed by the latter the process is not a very active one. That the polymorphonuclear leucocytes at times take up the bacilli in cases of human diphtheritic pseudo-membranous bronchitis we have already shown in our studies of the broncho-pneumonia of this disease.[11]

After the lapse of 18 hours the bacilli are found only with difficulty in sections, and in instances of still longer duration

*The lungs of the animal which lived 65 hours (Experiment 1) showed the greatest quantity of fibrin observed. The tissue which had been hardened in Flemming's osmic acid solution and stained in safranin was best adapted for the study of this material. The fibrin was found in fine threads and convoluted masses within the alveoli and the intralobular lymphatics. It was perhaps most abundant where the cellular accumulations were least marked.

*In this connection Miller's observation that lymph-vessels are not found in the structures of the lungs beyond the terminal bronchus is significant. The atria and air-sacs have no lymphatics in their walls.[18]

not at all. We did not discover the bacilli in animals which had lived 24, 47 and 65 hours respectively.

Bibliography.

1. Frosch: Die Verbreitung des Diphtheriebacillus im Körper des Menschen. Zeitschrift für Hygiene u. Infectionskrankheiten, XIII, 1893, 49.

2. Kolisko and Paltauf: Zum Wesen des Croups und der Diphtherie. Wiener klin. Wochenschrift, No. 8, 1889.

3. Wright: Studies in the Pathology of Diphtheria. Boston Medical and Surgical Journal, October 4 and 11, 1894.

4. Loeffler: Untersuchungen über die Bedeutung der Mikro-Organismen für die Entstehung der Diphtherie beim Menschen, bei der Taube und beim Kalbe. Mittheilungen aus dem Kaiserlichen Gesundheitsamte, II, 1884.

5. Kutscher: Der Nachweis der Diphtheriebacillen in den Lungen mehrerer an Diphtherie verstorbener Kinder durch gefärbte Schnittpräparate. Zeitschrift für Hygiene u. Infectionskrankheiten, XVIII, 1894, 167.

6. Wright and Stokes: A Report on the Bacteriological Investigations of Autopsies. Boston Medical and Surgical Journal, March 21 and 28 and April 4, 1895.

7. Belfanti: Sulle Broncopolmito Difteriche—studio batteriologico ed anatomo-patologico. Lo Sperimentale, XLIX, Sezione Biologica, 1895, 278.

8. Johnston: Notes on the Bacteriological Study of Diphtheria. Montreal Medical Journal, September, 1891.

9. Strelitz: Zur Kenntniss der im Verlaufe der Diphtherien auftretenden Pneumonien. Archiv f. Kinderheilkunde, XIII, 1891.

10. Booker: As to the Aetiology of Primary Pseudo-membranous Inflammation of the Larynx and Trachea, with Remarks on the Distribution of Diphtheria Bacilli in Organs of the Body distant from the seat of local Infection. Archives of Pediatrics, August, 1893.

11. Flexner: Diphtheria with Broncho-Pneumonia. Bulletin of the Johns Hopkins Hospital, IV, 1893, 32.

12. Kanthack and Stephens: The Escape of Diphtheria Bacilli into the Blood and Tissues. The Journal of Pathology and Bacteriology, IV, 1896, 45.

13. Hildebrandt: Baumgarten's Lehrbuch der pathologischen Mykologie, II, 1890, 455.

14. Flügge: Die Microorganismen, etc. Leipzig, 1886, p. 605.

15. Muskatblüth: Neue Versuche über Infection von den Lungen aus. Centralblatt für Bacteriologie und Parasitenkunde, I, 1887, 321.

16. Miller: The Structure of the Lung. Journal of Morphology, VIII, No. 1.

17. Baumgarten: Lehrbuch der pathologischen Mykologie, I, 406, Anmerkung 114, 1890.

18. Miller: The Lymphatics of the Lung. Preliminary paper. Anatomische Anzeiger, XII, 1896.

Winter, 1896.

THE BACTERIOLOGY OF PERTUSSIS.*

By Henry Koplik, M. D., *New York.*

Pertussis is a disease which has long been suspected or known to be communicable from individual to individual, and it is not surprising to find that various authors have approached the subject of its etiology in divers ways. The sputum seems to have been the principal subject of study, and bacteria and protozoa in the sputum have been selected, each in turn, as etiological factors. I need only mention the names of Deichler, Kurloff, on the one hand, Letzerich, Burger, Affanassjew, Ritter, Cohn and Neumann on the other, to recall to the mind a whole series of studies on the sputum, the one dealing with protozoan-like bodies in the sputum, the other with bacterial forms. In my own work, which has spread itself at intervals over several years, and lately culminated in the study of a series of cases of pertussis, I have directed my attention to the bacterial forms especially found in the sputum. I will not go into details here of my studies in other directions in this disease, such as bacterial studies of the blood, for they have led to no results. If we look over the literature mentioned above we may safely divide the communications on bacterial forms into two distinct sets: those which, like the work of Letzerich and Burger, were carried out without the aid of modern methods, and in which the instruments used were what we would call primitive; and those which can be judged to day, inasmuch as the methods employed were modern, such as those of Afanassjew, Szemetzchenko, Cohn and Neumann, and Ritter. Of those mentioned I will consider at length only the work of Burger and Afanassjew. Burger,* by means of a Seitz dry lens, 340 diameters, describes a bacillus or bacterium which he could easily see and which he calls biscuit form. He saw these in rows and chains and small rods twice as long as they were broad. He mentions distinctly that he found these bacteria in the flocculi of the sputum. It seems at this distance that it would be asking too much to decide just what Burger saw in the sputum of his cases, more especially as it is now known that both diplococci and bacilli of various varieties and size exist in this sputum. We miss unity in Burger's description. He did not isolate any one form, and from his description may have had several forms in his field when he studied the sputum, thinking they were all a single form.

Afanassjew's work appeared in the St. Petersburg Med. Wochen., 1887. Czaplewski and Hensel, who do me the great honor to agree with me in my conclusions, admit that

* Read before the Johns Hopkins Hospital Medical Society, February 21, 1898.

* Berlin. klin. Wochen., 1883.

they have not had access to the original work of Afanassjew. In view of this fact I will quote from Afanassjew's original article.

Afanassjew describes the sputum of pertussis as a transparent mucus in which are seen grayish white spots of the size of a pin's head. In the mucus of the sputum are seen bacteria and short, small bacilli, single or in pairs, at times in chains of no great length, arranged in the direction of the mucus of the sputum; at times in small groups. The length of these bacteria is 0.6 to 2.2 micro-millimeters, and are easily overlooked with low powers, and can only be distinctly seen with higher powers. "For this reason," says Afanassjew, "I doubt whether Burger has seen the bacterium described by me in the sputum, inasmuch as he says that he saw them distinctly with 340 diameters. I have made use only of powers magnifying 700 to 1000, with Zeiss ocular 3 and 4, and immersion $\frac{1}{12}$ with the tube drawn out." Afanassjew describes his bacteria as follows: "In gelatin, after two or three days, we find round or oval colonies, light brown with even borders, also oval colonies with a darker centre. The youngest colonies were almost colorless, but slightly granular, and did not fluidify the gelatin."

He also describes colonies of a thicker shorter bacillus, which in passing I may say may have been a contamination of his cultures. The bacillus described by Afanassjew grows at the temperature of the room, slowly, or more rapidly, at 38° C. or 37° C.

"*Agar stick culture* gives on the second day on the surface around the puncture a cloudy gray flat growth, transparent, glistening like a drop of fluid. In the following days the surface culture becomes more and more opaque and whitish gray."

"*Gelatin stick* gives a slower growth, thinner, on the surface flatter, grayish white with irregular edges; later on the edges become whiter and form a nail-head which is dry and rarely reaches to the periphery of the tube. The stick itself is not characteristic."

"*Blood serum* gives a grayish or whitish growth similar to the agar."

"*Potato gives rapid abundant yellowish, and after brownish growth.*"

"*In bouillon or hanging drop* we find the bacteria are alive, move very rapidly, inasmuch as they perform bobbing circular movements which soon cease."

"In the bouillon the bacteria grow in small threads."

I think in this article we may fairly leave out of consideration the work of Cohn and Neumann, and also of Ritter, which are chiefly concerned with the consideration of diplococci not clearly identified, and pass on to the recent work of Czaplewski and Hensel. The work of these authors was made known first through a preliminary communication in the Deutsche Med. Wochen., 1897, No. 37, and in the Centralbl. für Bacteriol., Dec. 22, 1897. They had worked upon over 44 cases of pertussis (an epidemic), in 18 of which they isolated what they call a polbacterium or bacillus, reminding one very much as to size of the influenza bacillus, if not smaller. The bacterium is, according to their view, not motile in itself. There was a slight motility in fresh bouillon cultures, which they were inclined to interpret as a Brown's molecular movement, but no independent movement of their own over the whole field of view. Gram stain did not decolorize fresh cultures, though it did the sputum.

The bacterium grew on Loeffler serum, agar, gelatin (non-fluidifying) bouillon, but *not as yet* on potato.

Loeffler serum gave an uncharacteristic grayish white growth; agar a delicate gray growth of transparent confluent colonies. On agar involution forms are described.

On gelatin it does not fluidify the medium, stick is not characteristic, and is made up of delicate whitish yellow granules like streptococci.

In bouillon we have cloudiness after a day and a sediment in the bottom, which on shaking resolves itself into thready slimy masses.

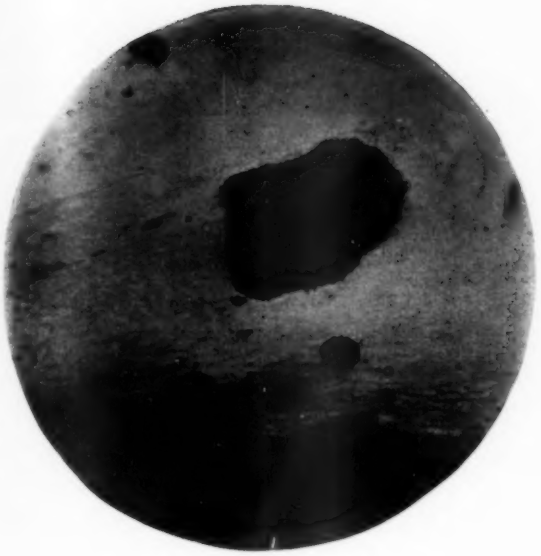
There is no mention in the work of Czaplewski and Hensel of the isolation of their bacillus in pure culture by means of plates and colony inoculation.

My own bacterial work on the sputum of pertussis was first read before the British Medical Association, in the latter part of August, 1897, and published subsequently in the British Medical Journal and the Centralblatt für Bakteriologie, 1897, Band XXII, Nos. 8–9.

In this communication I described a series of cases examined during the winter and spring of the same year. There were sixteen cases, and since then I may say I have been examining other cases with identical results.

The sputum was collected during a paroxysm of coughing in sterilized Petri dishes and allowed to stand a short while. The sputum separates in these cases into a glairy colorless mucus, in which are distinctly seen small grayish white particles like the scales of dandruff. These particles were fished out with a platinum needle, and *without* being subjected to further manipulation, such as washing, were sown in the media employed. In uncomplicated cases the above pellets of sputum are easily recognized, but if bronchitis or pneumonia complicates the case the sputum is more purulent and thick and does not separate as described. I also made use of hydrocele fluid, obliquely solidified at 65° C. to 70° C., in a transparent solid medium in test tubes, as my medium for cultivating this bacterium. I found and still think this medium especially fitted for the cultivation and isolation of the bacterium or bacillus described by me. I think this is due to the fact that hydrocele fluid is a poor medium for most bacterial species and favorable to the one interesting us. I made use of all the other media, but found that it was necessary to use the hydrocele fluid first to get the crude culture *en masse*, and from this to inoculate other media and make plates. I will not detail individual cases, as this has been done elsewhere, but will describe the bacillus isolated by me.

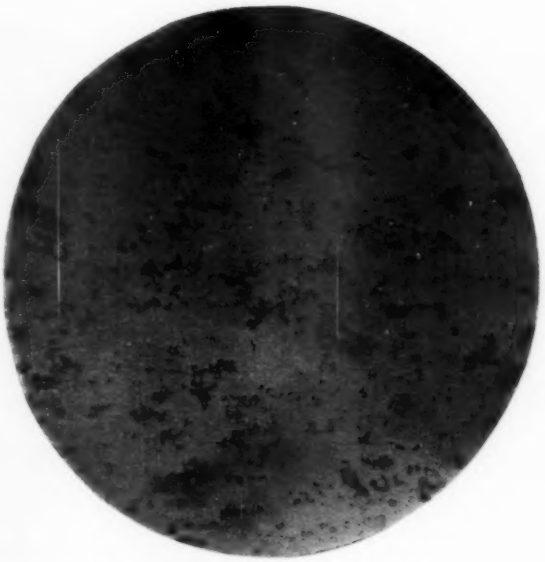
The Sputum. If a small grayish white pellet of the sputum of the convulsive stage described above is spread between two cover-glasses stained with Loeffler blue or fuchsin and examined, we see as a constant element a small exceedingly minute bacterium, either singly arranged in the direction of the striæ of the sputum or in small colonies; it may be seen in the epithelial cells or on the epithelial cells, or free, or in the meshes of the sputum. This bacterium or bacillus is so thin and



BACILLUS PERTUSSIS IN THE SPUTUM.

Fuchsin stain × 580.

Zeiss apparatus immersion $\frac{1}{12}$.



PERTUSSIS BACILLUS. PURE CULTURE.

Loeffler serum × 580 diameters.

Zeiss apparatus $\frac{1}{12}$ immersion.

small as to be quite easily overlooked even with a $\frac{1}{12}$ immersion, and in zoogloea it looks like a collection of cocci. Close study of the zoogloea reveals the fact of bacillary form. In cases not complicated by bronchitis or pneumonia these minute bacteria or bacilli are the only forms to be seen. As soon, however, as bronchitis or pneumonia sets in, other bacterial forms occur in the sputum and can be seen, and this will partly explain the difficulty of former workers in isolating this bacillus. If a small grayish pellet of the sputum be spread on obliquely solidified hydrocele fluid, or hydrocele fluid $\frac{3}{4}$ and glucose bouillon $\frac{1}{4}$, we obtain after a lapse of 24 to 48 hours in the incubator at 37° C. to 38° C. a mixed bacterial growth of a whitish or transparent gray color. A small part of this is suspended in bouillon according to Loeffler, and then a few platinum loops of the mixture spread on another hydrocele tube. In this way isolated colonies may be obtained, or agar plates may be made in the usual way from the whole growth. In this manner we find that the bacillus grows in pure culture on hydrocele fluid as a delicate grayish white or pearly growth. If sugar bouillon is added to the hydrocele fluid the growth is thicker, not so delicately transparent and more of a creamy color.

On agar we have at first a delicate grayish white growth, which in time becomes thicker and whiter and more opaque. If the agar is white and made with beef extract, the growth is very delicate, grayish and not so white. Colonies in agar are whitish or grayish white by reflected light, of a straw color or deeper olive tint by transmitted light. They are irregularly round or oval.

In gelatin there develops at the room temperature and quite slowly a fine granular stick, whitish, much like that of streptococci. It has a nail-head and does not fluidify the gelatin. Colonies in gelatin have a round or an irregularly round form, whitish yellow by reflected and straw colored or olive colored by transmitted light. They are finely granular. The colonies do not become very large.

In pepton bouillon we have a finely granular appearance after 24 hours and a cloudiness; after a time we have a sediment in the bottom of the test tube which is made up of small adherent masses. After a week or more the surface of the bouillon becomes covered with a thin sediment membrane which is made up of bacilli.

On Loeffler's diphtheria serum we obtain a whitish growth, reminding one much of the diphtheria growth.

On potato I have not as yet succeeded in obtaining a growth.

On human blood serum which is solidified on the surface of agar, we have a grayish white and abundant growth after forty-eight hours.

It should be here pointed out again that on agar the growth is delicate, grayish, transparent, and sometimes stops growing after a time, never being vigorous if the agar is clear and made of beef extract instead of beef juice. If agar is browner and made with beef juice the growth after a time is seen to be white, almost of an opaque pearly color; after a time, this difference in growth of agar tubes I could well convince myself of when recently working with pure culture obtained by plate colonies. This latter peculiarity will explain why Czaplewski and Hensel talk of a delicate growth on white agar when mentioning my agar appearances. Cultures and threads which have been allowed to stand in closed tubes for six months are found to be dead and cannot be reinoculated on other media.

The bacterium or bacillus which I have isolated in pure culture and which has the above cultural characteristics, grows anaerobic as well as aerobic.

If stained with Loeffler blue it appears as an exceedingly minute, delicate, thin, short bacillus form, much thinner than the diphtheria bacillus and not more than $\frac{1}{4}$ to $\frac{1}{2}$ its length. It measures 0.8 to 1.7 micro-millimeters in length, and 0.3 to 0.4 micro-millimeters in breadth. When stained with Loeffler blue it has a finely punctate appearance like the diphtheria bacillus, but here the resemblance stops, for it is a much more minute bacillus. In pure culture it is not decolorized by Gram stain. Old cultures on hydrocele and agar show club-shaped forms, the bacillus has a deeply tinged extremity like a club—in other words, involution forms exactly similar to the bacillus diphtheriæ. Of course the involution forms are exceedingly delicate and show much smaller than the bacillus diphtheriæ.

The name of "pol-bacterium" has been proposed for this bacterium by Czaplewski and Hensel in their article in the Centralblatt für Bakteriologie. The pol staining of this bacterium cannot be compared to such distinct pol-stain as that of a chicken-cholera bacillus (Kitt), rabbit septicæmia (bacterium bipolar), where the extremities of the bacterium are deeply stained and rounded, and there is a distinct square space in between the poles unstained. The staining of our bacterium is exactly identical with that of the influenza bacillus when stained in pure culture with method blue of Loeffler. The bacterium or bacillus of pertussis stains deeply at the extremities and there is an irregular space or two irregular spaces in the long axis of the bacillus unstained or lightly tinged when stained with methyl blue of Loeffler. Some of the extremities are rather swollen, most of the extremities or poles are round, others are lancet shaped. I have never been able to convince myself by any known methods that this bacillus has spores or flagella.

Motility. In my first communication I said this bacillus was motile. By this I simply meant that in the hanging drop it was seen to have a rapid bobbing circular motion in a very circumscribed area of its own. In some fresh bouillon cultures this very limited motion was active for a while and then ceased at the room temperature. I think that some would be inclined to deny that this was a movement inherent in itself inasmuch as the bacilli never traversed the microscopic field. I am quite willing to admit that this movement might be classed with cocci movements (Brown's molecular movements).

Animal Experiments. In my first paper I showed how fruitless animal experiments with this bacillus were. It is pathogenic to mice in large amounts of a $\frac{1}{2}$ to 2 cc., but in no instance was I able to reproduce symptoms of a disease similar to whooping cough in the lower animals. I think as I did then that accidental inoculation of the human subject could alone enlighten us. It would be going too far to make any such experimental inoculations.

From the above it will be seen that from the sputum of pertussis cases in the convulsive stage, Czaplewski and Hensel and I, independently of each other, have isolated pure for the first time a bacterium which is constant and found in no other sputum. This bacterium is especially characterized by a minuteness comparable only to the influenza bacillus (Pfeiffer) or that of septicæmia of mice (Koch). In staining the dotted (not granular) appearance spoken of by me and compared to that of the bacillus of diphtheria, can best be brought out by the Loeffler alkaline blue stain. Fuchsin stains more coarsely and more uniform. The swollen end forms, or as I call them the involution forms, can also be brought out by Loeffler blue stain. I wish to point out here also that both in my first paper and in this I worked with pure cultures only (obtained by means of plate colonies). In this perhaps we find a reason why authors who have preceded the communications of myself and Czaplewski and Hensel differ so widely in what they saw. They failed to obtain the bacterium in pure culture. It may be remarked in passing that in my second cases as well as in some of my first cases there could be found among other bacterial forms a bacillus closely resembling the bacterium isolated in this work. This latter is somewhat thicker, grows in longer chains and fluidifies gelatin. I am inclined to think that observers have hitherto been much baffled by this bacillus, which I think with Czaplewski and Hensel is simply accidental. Such must have been the case of Cohn and Neumann.

I have tried to isolate my bacillus or bacterium in the early stages of pertussis before the convulsive paroxysm has appeared, and have not succeeded thus far in separating it from the saliva.

What significance can we attribute to the bacterium which is the theme of this paper? I doubt whether this can be solved except by direct experiment on the human subject. I may not be going too far to predict that the bacterium will aid us in understanding the mode of contagion in pertussis. It may be the first definite step in showing that in the sputum of the pertussis sufferer lies the danger of the communication of the affection to others.

Discussion.

Dr. Osler.—I would ask Dr. Koplik if he has followed a case through from beginning to end and whether there is any difference in the abundance of bacilli during the early and late stages. Some have held that the disease was more infectious in its early stage.

Dr. Koplik.—I would say that I have tried to make a diagnosis of pertussis before the convulsive stage appeared. I could not find the bacillus in the mouth. The bacilli seem to be most abundant in the convulsive stage, but I did not follow up the study to see whether they persisted in the stage of convalescence.

Dr. Welch.—I notice that Dr. Koplik spoke of the staining in his first paper as granular, and Czaplewski supposes that he means polar staining. In Czaplewski's photograph the polar staining is none too definite, and he uses almost altogether carbolic-gentian-violet, which gives an irregular staining with many bacteria. I would ask if this is a polar staining like that of chicken cholera, or an irregular staining as of the diphtheria bacillus.

Dr. Koplik.—I would classify it as more like the irregular staining in diphtheria. I think that the bacteria are more like the diphtheria organism than a real polar bacteria.

Dr. Sternberg.—It seems to me that the photograph does not show an extremely minute organism such as the influenza bacillus for example.

SUPPLEMENTARY REPORT ON THE STERILIZATION OF INSTRUMENTS BY FORMALDEHYDE.

By H. O. Reik, M. D.

The December number of this Bulletin contained an account of the work performed by Dr. Watson and myself with formaldehyde gas, and we stated then that Meyrowitz of New York was making for us an apparatus especially adapted for the use of this method of sterilization. The accompanying cut represents the sterilizer referred to and which I am now using in my daily work. It is of a size suitable for the ophthalmologist, otologist, laryngologist, or other surgeon who uses comparatively small instruments. Should the general surgeon or the obstetrician desire to adopt the method, a larger sized sterilizer can be readily made and special appliances may be inserted for holding the particular instruments used by him; as for instance there is figured in the illustration a small tray for carrying such delicate instruments as the cataract knife, etc., so as to prevent their cutting edges from coming into contact with anything.

The sterilizer which I have adopted for myself is 7x12x12 inches, giving an air space of a little more than 1000 cubic inches. The shelves are made of heavy, wide-meshed wire gauze, the upper one extending entirely across the chamber, while the lower two are only eight inches long, extending from the right side to an upright standard four inches from the left wall, thus leaving a space four inches wide by eight inches high which is reserved for the Schering lamp used in vaporizing the pastilles.

In the report of our work we called attention to two features in the sterilization of instruments by this method which we thought required further study. The first related to the question of the deposit of paraform on the instruments and the possibility of such a deposit retarding the healing of wounds. The second was the possible effect of the gas upon the cutting edge of the instruments.

I think we are able now to give positive answers to both problems. Since receiving my new apparatus I have repeated all the bacteriological experiments quoted before and with the same results published. I have further exposed instruments to five and six successive sterilizations by the gas, without any washing or cleansing whatever, and at the end of the experiments I was not able by the naked eye to discover any deposit whatever, nor was there any taste of the gas when the instrument was applied to the tongue. A cataract knife so exposed was used in making a corneal section on the rabbit. Healing of the wound took place as usual when a sterile knife is used. Blunt instruments so exposed and then applied to my own conjunctiva produced no irritation.

As to the question regarding the edges of the knives, I tested very carefully their sharpness by means of the kid drum, both before and after sterilization, and I am not able to discover that the gas affects this in any way. To see whether or not the gas would affect instruments made of other material than steel, I repeatedly exposed the following instruments to the action of the gas: knives with aluminum handles, knives with ivory handles, a hard rubber syringe, soft rubber catheters, a Politzer air bag, and a nickel-plated syringe. None of these objects were in any way affected by the gas.

My conclusions are then that we have in this method a rapid, cheap, easy and sure method of sterilizing instruments without in any way injuring them.

CORRESPONDENCE.

DOES WILHITE'S STORY OF THE NEGRO BOY INCIDENT IN THE DISCOVERY OF ANÆSTHESIA "LACK PROBABILITY"?

Letter from Dr. Wilhite.

To the Editor:—

My attention has been called to the article published in the August and September issue of this Bulletin from the pen of Dr. Hugh H. Young, Assistant Resident Surgeon Johns Hopkins Hospital, entitled "Long the Discoverer of Anæsthesia."

The writer has in a very interesting manner restated a part of the much discussed history of anæsthesia. I shall then not tax the reader's patience by another recital. Having been an interested spectator as well as a listener at the semi-centennial in Boston, October 16, 1896, of the *alleged* first discovery of anæsthesia—at which meeting quite a number of distinguished men of the medical profession, representing different parts of the United States and elsewhere, demonstrated to *their* entire satisfaction and others that Morton was entitled to the glory *alone* of this discovery—I would have been content to let the matter rest, so far as I am interested, but for the article of Dr. Young, wherein some reflections are cast upon the memory of my deceased father, Dr. P. A. Wilhite, whose statements in New York, 1876, gave rise to the article of Dr. J. Marion Sims, published May, 1877, in the Virginia Medical Monthly. From my youth I have been conversant with the facts as related by my father; and as he was the life-long friend of Dr. C. W. Long, as well as an enthusiastic supporter of Long's claims to the discovery of anæsthesia, I have been puzzled to understand why *twenty years* after Dr. Sims' article has appeared, and after Sims, Long and Wilhite have passed beyond the realm of controversy, labored efforts should now be put forth to throw doubt upon Wilhite's statements that first awakened interest in Long's claim, when the only errors of which Dr. Long himself complained to Wilhite were the mistake made in the date when he and others entered Long's office, and of being present at the first or second operation by Dr. Long, and of saying that the first inhalation of ether in Jefferson was before the same persons. Dr. Young is charitable enough to admit that Long never mentioned this incident as being one of the mistakes in Wilhite's statement. I feel that injustice to the memory of Dr. Wilhite has been done, and that I ought not to permit some of the statements made by Dr. Young on this subject go unnoticed.

In a private letter from Dr. Young I am led to believe that it was not intentional on his part to do injustice in the matter to Dr. Wilhite, and that "his information came largely from papers of Dr. L. B. Grandy, of Atlanta." Since his information comes from Dr. Grandy, whose article was published in the Virginia Medical Monthly, 1893, and since he has courteously invited me to criticise his article and present documentary proof concerning Dr. Wilhite's claims, I will not be regarded a naked trespasser in this fertile field of controversy. Now, let me state at the outset, Dr. Wilhite never claimed to be the discoverer of anæsthesia, *only so far as being the first one to produce the full anæsthetic effect of sulphuric ether accidentally*, and it was only at the earnest solicitations of friends that he placed himself before the medical profession in 1883 to receive such honor as might be due him; neither did he in any way seek to detract one iota from the honor he believed justly due his old preceptor and friend, Dr. Long. What he claimed then was that on one occasion while a boy at a country frolic in Georgia, he with others caught a negro boy, and while the others held the boy, he (Wilhite) administered to him sulph. ether, rendering him unconscious, etc., so much so that a doctor was sent for to revive the negro boy, and that when studying medicine under Dr. Long he related to him the circumstance. It would seem from recent attacks that Dr. Wilhite's *offending* consisted mainly in making a statement from "*recollection*" to Dr. Sims in New York that he was a student under Dr. Long and witnessed the first operations, and further, when a boy about seventeen years old he accidentally etherized a negro boy at a frolic in 1839, when the

year, as we shall see, was 1841. In order to make it appear that the story "lacks probability" the date of a letter is shuffled from January 27, 1877, to June 27, 1877, which Dr. Young states is a reply to a letter from Dr. Long, of May 20, 1877, and his daughter is quoted as giving the information that her father "repeatedly told her that he had never heard of it before it appeared in Sims' article." (I shall now take the liberty to refer to his (Dr. Y.) source of information by reference to Dr. Grandy's article, etc.) Dr. Grandy in his article, speaking of Mrs. Taylor's statements, says: "She tells me that the above story *was related* (italics mine) to Dr. Long by Dr. Wilhite *himself* in the presence of several of the family, when Wilhite was on a visit to her father's house in the *spring* (italics mine) of 1877. After hearing it, Dr. Long replied, "Doctor, this is the first time I ever heard of it." Now I submit that Dr. Wilhite's visit to Long, in Athens, was after the publication of Sims' article. Dr. Young says: "The ether controversy was never re-opened and Long's work was unknown to the world until 1877, when J. Marion Sims, hearing of him *through accident* (italics mine), investigated his claims, was fully convinced of their merit, and vigorously demanded their recognition by the medical profession. His paper appeared in the Virginia Medical Monthly, May, 1877." Then he says again: "This article which obtained for Long the first recognition of any consequence was the outcome of a conversation which Sims had with *a Dr. P. A. Wilhite, of Anderson, S. C.* (italics mine). He summarizes the statements of Wilhite to Sims, and adds: "*Dr. Sims at once communicated with Dr. Long and soon convinced himself of the truth of his claim, but unfortunately failed to investigate Wilhite's satetments, but embodied them in full in his article, giving Wilhite the credit of first intentionally producing profound anæsthesia with ether*" (italics mine). How does Dr. Young know that Dr. Sims never investigated the negro boy story? Does he not state: "Sims sailed for Europe soon after the publication of his article, and Long died in a few months, and Wilhite's statements went unchallenged for many years"? Let us see what Grandy said in 1893. "Sims' article appeared in May, 1877, and Long at once noticed the errors and the absence of promised corrections. He requested Sims to correct the mistakes, but the latter replied that the 'misplacement of a few names and dates would not alter the main facts in the case.' He sailed for Europe in a few days and the matter was dropped." Now as a matter of information and to know when Sims did sail for Europe, I have in my possession a letter from his son which reads as follows:

NEW YORK, September 28, 1897.
30 West 58th Street.

My Dear Doctor:—On account of my absence from the city your letter of the 21st instant was not received until to-day. In May, 1877, my father was to have sailed for Europe on the Celtic. . . . . He and I went to San Francisco in June of that year. He returned here and sailed for Europe some time in July, about the latter part. . . . Believe me, yours sincerely,

(Signed) H. MARION SIMS.

Why would Sims have needed to investigate Wilhite's statements further than to write to Long for the facts? Did not Long send them? See the letter hereinafter quoted. Dr. Young further states: "The negro boy story lacks probability, as Wilhite did not enter Long's office until 1844, two years after the first operation, as the following letter from Long to Wilhite shows." Now I admit that the letter shows this: Wilhite did not enter Long's office until 1844 and therefore he was not a student in his office in 1842 when the first operations were performed. I challenge Dr. Young to point to one word or sentence in that letter *quoted* to show that the negro boy story "lacks probability." In order that the reader may see the point I make, I quote the letter as published by Dr. Young:

ATHENS, GA., May 20, 1877.

DR. P. A. WILHITE.

Dear Sir:—I received Dr. Sims' article on anæsthesia yesterday and find several mistakes. Dr. Sims states that yourself, Dr. Groves and Drs. J. D. and H. R. J. Long were students of mine and witnessed the operation performed on Venable, 1842. Your recollection failed you at this time, as it was several years, at least two, before either entered my office. You will see that you were mistaken in giving Dr. Sims this information. You also make a mistake in saying that the first inhalation in Jefferson of ether for its exhilarating effects was before the same persons. . . . I wrote to Dr. Sims informing him of the errors and asking him if he considered the mistakes of sufficient importance to be noticed, etc.

(Signed) C. W. LONG.

Dr. Young has the candor to say, "In the letter to Wilhite, Long makes no comment upon the negro boy incident." Then why should he say it "lacks probability" from *that* letter? He, I submit, does injustice by quoting a letter of Dr. Wilhite in that connection to Dr. Long, making it appear that the letter bore date June 27, 1877, and states that it was a reply to Dr. Long's letter of May 20, 1877. I will quote this letter later on in its proper connection, and I am satisfied that he will see its inapplicability to his assertion. Now his proposition is that the negro boy incident "lacks probability." That is the question at issue and he has assumed the affirmative, and the burden of proof rests upon him. I am not called upon to prove a negative. The only thing he has relied upon is the letter quoted and the statements of Dr. Long's daughter, "but his daughter informs me that he repeatedly told her that he never heard of it before it appeared in Sims' article." Before impartial judges I submit he has not made out his case and established his proposition. The letter does not do it, for even admitting for the sake of argument that Long never heard of it until he saw it in Sims' article, or never heard of it *himself* as told to him in the spring of 1877, does not establish its improbability. I might rest the matter here but for the imputation cast upon Dr. P. A. Wilhite's veracity by the proposition, and this I must be permitted to defend. It needs none in South Carolina where he was known, but your BULLETIN is not local. It goes among gentlemen who did not know him. It is true that he was a country physician; but in this dawn of the twentieth century the old Pharisaical question, "Can anything good come out of Nazareth?" should be discarded and the Nazarene's command, "Render unto Cæsar the things that are Cæsar's," should take its place.

"Honor and fame from no condition rise; act well your part, there all the honor lies," might have been justly said of Dr. P. A. Wilhite in his limited sphere of action. He spent his life in

the interest of suffering humanity, and when the summons of death came, June 25, 1892, "he wrapped the drapery of his couch about him like one who lies down to peaceful dreams." Neither envy of men nor their sneers will disturb his repose. He eschewed politics and practiced medicine in Anderson, S. C., for nearly forty years upon his merits. The *People's Advocate*, a newspaper published in the city of Anderson, June 27, 1892, said: "In the death of Dr. P. A. Wilhite, Anderson loses one of her best citizens, liberal and progressive in his nature and upright in character. . . . He was one of our most noted physicians, was esteemed by all classes, and the whole city is in sorrow over his death." . . . The *Anderson Intelligencer* said: "Dr. P. A. Wilhite, one of the oldest and most skillful and most highly respected physicians in this portion of South Carolina, departed this life at his residence this morning. . . . In 1878 Dr. Wilhite was appointed a member of the State Board of Health, then created by act of the Legislature of this State, and remained an active and influential member of the Board until his death." . . . . I might add further extracts from the press, etc.; suffice it to say that neither of these notices was written by relatives, but such is a part of testimony and tribute paid his memory publicly by those with whom he lived and for whom he lived for upwards of forty years. He was born in the State of Georgia about two miles of Danielsville, June 6, 1822 ("Dr. Long in Danielsville"), Dr. Long being about seven years his senior. Dr. Grandy says, "Up to the time of Dr. Long's death the relations between himself (Dr. L.) and Dr. Wilhite appeared to have been very friendly." His daughter had stated that Dr. Wilhite was a visitor to Dr. L. in the spring of 1877. The writer well remembers this visit, as he was an inmate of Dr. Long's house for a long time as a boarder, was then a student in Athens and was frequently in Dr. Long's private place of business, as well as a visitor in the family circle, and he knows of his own personal knowledge that the relations of the two men were friendly and cordial. This was before and after Sims' article appeared, and therefore I insist the letter quoted by Dr. Young from Wilhite to Long as of June 27, 1877, is incorrect, for it was not far from about that time when Wilhite visited Long. During this visit I was with my father and Long a great deal of my time and heard them discussing the facts, and to the best of my recollection there was no disagreement as regards the negro boy incident. The letter quoted by Dr. Young from Long to Wilhite shows that Long had then (May 20th) received and read the article, had written to Wilhite about the inaccuracies of dates and persons present, and had never once mentioned the negro boy incident, as Dr. Y. says. The reader will observe the . . . . (omission) in the letter quoted. Just what was left out I do not know. Until Dr. Grandy's article appeared the statement of Wilhite has not been questioned so far as I know by Long's friends. That Wilhite enjoyed the personal friendship and esteem of both Long and J. Marion Sims is abundantly shown by the visits paid them and their private letters still in our family.

That Wilhite was mistaken as to the true date of etherizing the negro boy, and as to the time he entered Long's office, there is no doubt. He made the statement from *memory* after a great number of years in a casual conversation without any *memoranda* before him. Now let me quote some of the correspondence that bears on this subject:

267 Madison Ave., New York,
January 12, 1877.

My dear Dr. Wilhite:—I wrote to Dr. Crawford W. Long, of Athens, three weeks ago, asking him to give me some notes of himself and special data about his discovery of ether as an anæsthetic. He does not reply to my letters. Will you have the kindness to write to him and say that I am to prepare a sketch of his life for Johnson's Cyclopedia and would like to have all the facts as soon as possible. Please help me in this matter, and with kind regards to all, believe me, dear Dr. Wilhite,

Most truly yours,
(Signed) J. Marion Sims.

Admitting the genuineness of the letters published by Dr. Grandy, Dr. Wilhite wrote upon receipt of this letter as follows:

Anderson, S. C., January 16, 1877.

Dr. C. W. Long.

Dear Doctor:—I have just received a letter from Dr. J. Marion Sims of New York, stating that you will not write to him, or at least that he wrote to you about three weeks ago and received no reply. If you don't do so soon it will be too late. He has been preparing an article for publication, and wants to place you right before the world. You have been apprised, I suppose, of the nature of the article. Why you have been connected with, and will be the leading spirit in the article, *happened* (italics mine) *in this way: While I was in New York last summer at one of Dr. Sims' private operations, several prominent physicians being present, I happened to remark that I witnessed the first or second operation ever performed under an anæsthetic. Every one said I was mistaken, and particularly Dr. Sims . . . . After that I met Sims at his office and gave him such particulars as I could recollect of your first operation* and also urged your claims to the priority. He at once wrote you on the subject and has since become very much interested in the matter. Now, Doctor, *it is but justice to you* (italics mine), as it is due the world, that you give Dr. Sims such information as he asks for at once, as he is going to all this trouble only to place the proper credit of this great discovery on the man who justly deserves it. I honestly hope you will comply with the Doctor's request as soon as possible . . . . As I have been the means of giving this investigation of this subject its present shape, I am exceedingly anxious that you should give all the information you can, that you may, and justly too, receive the credit of this great discovery. If you will act it will certainly be so. Dr. Sims also wants a short history of your life, which don't fail to give. Hoping to hear from you, I remain,

Yours, etc.,
P. A. Wilhite.

I have italicized some of the letter to call attention to the fact that Wilhite was urging Dr. Long to give the facts. The reader will notice that in publishing this letter Dr. G. did not publish it all, as shown by the . . . . in two places. Dr. G. says to that long letter Dr. Long replied. Here is a copy of his reply never before published and is in my possession:

Athens, Ga., January 22, 1877.

Dr. P. A. Wilhite.

Dear Sir:—Your welcome letter of the 16th instant was received a few days ago and I have been too busy to answer it earlier. I regret that my situation was such that I could not write to Dr. Sims earlier. I made a full explanation in a note mailed him before yours was received. *This morning in sending off some certificates* obtained some years since I find a number lost, yours among

the number. Now, Doctor, I wish to obtain yours again as early as possible to send to Dr. Sims.

I see from your letter that you stated to Dr. Sims and other physicians that you witnessed an operation by me under an anæsthetic before any published account of the use of ether to produce this effect.

My recollection is that you entered my office late in 1844, and that early in January, 1845, you were present and witnessed me perform an amputation of a finger of a negro boy belonging to Ralph Bailey, Sr., the boy etherized at the time. I am not positive this was the operation, but as I have the certificates of Mr. Bailey and his son and sons-in-law, who were present at this operation, I think this must have been the operation you alluded to. I have mentioned these facts to refresh your memory if you have forgotten names and dates. The correct date of the operation was 8th of January, 1845. If this was the operation alluded to you can from these circumstances give correct report of the operation.

You may recollect some other operation; if so, state the facts in regard to it . . . .

Permit me to thank you for the interest you take in establishing my claim. If it is established you will have been the mover in it. (Italics in this letter mine.)

Yours respectfully,
(Signed) C. W. Long.

Admitting the letter as published by Dr. Grandy, Wilhite replied. I will put this letter in a parallel column with the letter Dr. Young quotes as being written June 27, 1877, in reply to Dr. Long's letter of May 20, 1877.

(Young)

Anderson, S. C., June 27, 1877.
Dr. C. W. Long.

Dear Doctor:—Yours of the 22nd instant is at hand, and I have also just received a letter from Dr. J. M. Sims which I will answer to-day . . . .

In my statement I did make a mistake in regard to my being present at the first or second operation, which mistake I will correct. But if you still prefer I will send a certificate . . . . Let me know and I will give you any information or assistance in this great matter.

Yours truly, etc.,
(Signed) P. A. Wilhite.

(Grandy)

Anderson, S. C., Jan. 27, 1877.
Dr. C. W. Long.

Dear Doctor:—Yours of the 22nd is at hand, and I have also just received a letter from Dr. Sims which I will answer to-day. In regard to the certificates you spoke about it will not be necessary, I think, as Dr. Sims has my statement written out in full. He was particular to get all the points and facts I could recollect.

In my statement I did *make a mistake about my being present at the first or second operation, which mistake I will correct* (italics mine, L. B. G.).

If you still think proper I will send a certificate. Let me know and I will give you any assistance in this great matter.

Yours truly,
P. A. Wilhite.

I think when Dr. Y. takes the letter of Sims to Wilhite, dated January 12, 1877, Wilhite's letter to Long, dated January 16, 1877, Long's letter in reply to Wilhite's, dated January 22, 1877, and Wilhite's letter to Long, January 27, 1877, in reply to the 22nd letter, he will perceive at a glance that Wilhite could not have written a letter June 27, 1877, in reply to the letter May 20, 1877. The internal evidence of the letter and the connection show this.

Sims' article had been published before May 20th, and why should Wilhite a month afterwards (June 27, 1877) be writing in reply "yours of the 22d instant"? Did Long write to Wilhite, June 22, 1877? We have no such letter in the correspondence. Then it would have been a remarkable coincidence for Long to have written January 22nd and also June 22nd, and for Wilhite to have answered January 27th that he had just received a letter from Sims which he would answer that day, and also June 27th in the same words.

After all this correspondence I must be pardoned for again asking the question, How does Dr. Young know that Sims never investigated the Wilhite statements? Upon what hypothesis does he rest his proposition that the story of the negro boy "lacks probability"? The proof is not shown in the published letters. Whether Wilhite told Long about the negro boy incident or not, was it a fact? Dr. Sims accepted it as a fact on Wilhite's own statement. It was sufficient with him, and it would have been sufficient with his old friend and preceptor Long. Has not Long requested him to give any additional operation and extended his thanks for his interest, etc.? But these men are all dead and gone. Wilhite (seemingly) being an obscure country physician, it is proposed to brush away in a flippant manner his statements from the record. I submit to all unprejudiced minds that it is immaterial, as Sims said to Long about certain dates, whether Wilhite was a student in Long's office in 1842 or 1844, so far as the facts of Dr. Long's work is concerned; whether Wilhite was seventeen years old or nineteen years old; whether it was 1839 or 1841 when he accidentally etherized the negro boy. The sole question is, did he do it the last year mentioned?

Dr. Young says that unfortunately Sims did not investigate Wilhite's statement. Then what did Dr. Sims write to Dr. Long for the facts for? Why did he write to Wilhite to urge Long to send all the data or facts? Why did Long ask Wilhite to mention any other additional operation? Suppose Sims had carefully investigated Wilhite's statements independently of his personal confidence he had in his veracity, what would have been the result of the investigation? Fortunately for the memory of Dr. P. A. Wilhite, the South Carolina Medical Association appointed three of its honored body, Dr. J. R. Bratton, Yorkville, S. C. (died 1897), Dr. B. W. Taylor, Columbia, S. C., and Dr. C. R. Tabor, Fort Motte, S. C., a committee to investigate the matter. Upon the advice of friends, there still being living witnesses to that incident in no way interested in the matter, Wilhite procured their affidavits, which, with his own statement under oath, he produced before the committee (Trans. S. C. Med. Ass., April, 1883). The original affidavits of his witnesses are now in my possession, and they were not written by Wilhite to fit his case. Fac-simile or photograph copies can be procured if Dr. Y. doubts my statement. Upon this testimony the committee made its report to the S. C. Medical Association, 1883, and published in its proceedings. This is a copy of the affidavits:

I hereby certify that in the year 1841 (exact date I do not remember) I did administer to a negro boy, about twelve years of age, sulphuric ether until he was completely anæsthetized, in which condition he remained for more than an hour. This occurred at the residence of Mr. J. N. Wier, in Clark County, Georgia. It was customary in those days for the young ladies and gentlemen to

congregate and have what were called ether frolics. It was on one of these occasions that I administered the ether to the negro boy, who was held by Mr. Robert Wier. I administered the ether on a towel until the boy became fully anæsthetized. When this happened we all became very much alarmed at his condition, he being perfectly insensible, with a slow and stertorous breathing. Nothing that we did aroused him—slap him, pinch him, roll him over, etc.; so we came to the conclusion that we had killed him. Dr. Sidney Reese, who lived five miles away, was despatched for immediately. The doctor came in about an hour and a half, during which time the boy displayed very little evidence of waking up. After the proper means were applied he was aroused from his state of insensibility.

Personally appeared Dr. P. A. Wilhite before me and makes oath that the statements herein made are correct according to the best of his recollection.

Sworn to and subscribed before me, at my office, Anderson County, S. C., this the 29th day of May, 1883.

John W. Daniels, P. A. Wilhite.
Clerk of Court Common Pleas,
Anderson County, South Carolina.

This testimony of Dr. P. A. Wilhite is fully corroborated by the affidavit of Samuel B. Wier, which is as follows:

State of Georgia, }
Jackson County. }

I hereby certify that in the year eighteen hundred and forty-one I was present and participated in a social collection of young gentlemen and ladies at John Wier's, at what was called an ether frolic, and on that occasion I saw a negro boy put to sleep with sulphuric ether, administered by P. A. Wilhite, one of the young men present, now Dr. P. A. Wilhite, of Anderson, S. C. The boy was held by Robert Wier, while Wilhite gave the ether, until the boy became unconscious. The boy remained in that condition for some time, and not waking up, as they thought he should, and breathing very heavily and being perfectly limber, the party became alarmed, believing that Wilhite had killed the boy. A physician was sent for, who arrived in about two hours. Up to that time the boy had shown but little evidence of waking up.

Dated December 11th, 1882.

(Signed) Samuel B. Wier.

I hereby certify that I was present when the above certificate was signed by Samuel B. Wier. I have known him for twenty-five years and know him to be a gentleman of honor and truthfulness.

(Signed) Green R. Duke,
Dept. U. S. Marshal.

State of Georgia, }
Jackson County. }

I, J. L. Williamson, Clerk Superior Court of said county, do hereby certify that S. B. Wier is a citizen of said county and that I know him to be a gentleman of honor and truthfulness.

Dated December 11th, 1882.

(Signed) J. L. Williamson,
Clerk S. C.

State of Georgia, }
Clark County. }

I, the undersigned, hereby certify that I was present in the year 1841, the exact time not recollected. A collection of young people met at my house for the purpose of having a little fun and an ether frolic, and on that occasion a negro boy was put to sleep with sulphuric ether, administered by P. A. Wilhite, one of the young men present, now Dr. P. A. Wilhite, of Anderson, S. C. The boy was held by one of the young men, and the ether was administered until the boy became perfectly unconscious. Remaining in that condition for some time, and showing no signs of waking up, and breathing very heavily, we became alarmed, believing that Wilhite had killed the boy. A doctor was sent for, he (Dr. Reese) arrived in about two hours, and up to that time the boy had shown but little evidence of coming to consciousness.

Dated December 12, 1882. (Signed) Mrs. L. C. Wier.

I hereby certify that I was present when the within certificate was signed by Mrs. L. C. Wier. I have known her for fifteen years and she is a lady of high standing and unquestionable veracity.

December 12, 1882. (Signed) Green R. Duke,
Deputy U. S. Marshal.

(The committee of the S. C. Medical Association omitted by oversight this last certificate and omitted giving the full name of Mrs. Wier.)

In conclusion let me say I have tried to avoid saying anything that might appear personally offensive to any of the profession or any one connected therewith. I have claimed the liberty to insert in this statement certain points made by Dr. G., showing the errors of the article of Dr. Young, for each claimed to have access to private papers of Dr. Long.

Dr. Wilhite *never* by word, deed or act, privately or publicly, sought to claim any honor in this matter for the boyish frolic, etherizing the negro boy in 1841, except what was justly due him; neither do I; and as he, if living, would not seek to pluck one leaf from the laurel of Dr. Long, neither will I seek to rob him or any one else who may have a better claim to the crown. I submit that if human testimony of disinterested witnesses has still any weight or force with gentlemen in the forum of discussion, then no one ought to rise up and make the assertion that Wilhite's statements "lack probability." It was not a figment of his imagination, but a veritable fact. Dr. Long lived over a year after the statement of the negro boy incident as published in Sims' article, and continued in the harness up to his death. If he discredited the statement, he lived in Georgia but a few miles from the place where the incident was stated to have occurred. If it had been a fake, how easy would it have been for him to have gotten the testimony to establish its incredibility had the story been untrue.

With this I must leave the matter where Dr. Sims left it, having faith that an unprejudiced profession as well as the public will in the end render a righteous verdict and see as I do that for his labor of love for Long there is in return now ingratitude.

J. O. Wilhite, M. D.

125 North Main Street, Anderson, S. C., November 1, 1897.

Letter from Dr. Young.

To the Editor:

In the paper of Marion Sims, Wilhite is quoted as saying that previous to the discovery of anæsthesia by Long he was a student in Long's office; that when Long was discussing the possibility of producing anæsthesia with ether, he "encouraged him" by relating how he had unintentionally etherized a negro boy; and when Long, thus persuaded, did administer ether to Venable and operate on him, he, Wilhite, assisted in the operation; thus modestly taking to himself a large part of the credit of the "great discovery."

The papers in my possession show conclusively that Wilhite did not enter Long's office until two years after Long's discovery; that he was not present at the first operation; that he

was a boy younger by seven years than Long, and therefore probably not Long's confidant and adviser.

The only remaining statement was the story of etherizing the negro boy, which Wilhite claimed to have done in 1839.

Numerous witnesses testified that the custom of inhaling ether in that part of Georgia began in the winter of 1841 and 1842 and was originated by Long, who had learned of the exhilarating properties of ether at the Medical College in Philadelphia, at least two years later than Wilhite, then a young schoolboy, claimed to have used it.

To say therefore that "the negro boy story lacked probability" seemed to be putting it mildly.

My conviction was further strengthened by finding that L. B. Grandy, first in an article in the Virginia Medical Monthly, October, 1892, and again in the New York Medical Journal, July 20, 1895, had vigorously attacked Wilhite's statements, declaring that they were "fiction, pure and simple—*falsus in uno falsus in omnibus*," and no one, not even his son, had contradicted Dr. Grandy. Was I not justified therefore in assuming that it was an acknowledged fact that the negro boy story lacked probability? I think so.

Permit me to add that the unimportant inaccuracy of date in my paper, which he attributes to most sinister motives, was due merely to the indistinctness of the manuscript. After debating for a long time I decided that the word was intended for "Jun." and not "Jan.," a mistake, as it now appears, but of no practical import.

Dr. Wilhite's paper is valuable because he brings witnesses to prove that his father really did unintentionally, but nevertheless actually, etherize a boy to complete narcosis, a very interesting point in the history of anæsthesia. But that he had absolutely nothing to do with the discovery of anæsthesia by Long in 1842 must still be considered certain.

HUGH H. YOUNG.

NOTES ON NEW BOOKS.

The American Year-Book of Medicine and Surgery. Edited by GEORGE M. GOULD, M. D. (*Philadelphia: W. B. Saunders*, 1898.)

The excellence of the editorial work done by Dr. Gould is so often exhibited and so well recognized that but few words of praise are needed from us for this work.

Although there has been some change of collaborators since the last Year-Book appeared, there has been no falling off in the work done, and all the assistants should be congratulated for their help in producing so useful a book and one which requires so much care and labor to make it of value.

As time advances the editing of this Year-Book will become more and more difficult, for there is a large increase yearly in medical articles and journals. This makes a proper selection harder and harder, and as the personal equation must enter into such selections, they become in a certain degree less and less valuable. No one knows beforehand what apparently insignificant point in some article may prove of significance before the next year is passed, and so articles may be omitted from consideration which a year later will prove to have been really important contributions. To remedy this, we believe lists of articles which have not been touched upon on all important branches should be appended at the end of each chapter. This scheme may not be feasible, but if some such scheme is not devised, the value of the Year-Book, which is, after all, only that of a good reference book, will diminish yearly. Had we "Centrallblätter" in this country there would be less need of a Year-Book, and these "Centrallblätter" have their distinct advantage in being to a greater or lesser extent limited to special branches of medicine, surgery, etc., so that the practitioner is not obliged to purchase a large Year-Book, only a portion of which interests him, but with his "Centrallblatt" is able from week to week to pursue any special subject in which he may be interested. Why would it not be possible to publish the several sections of the Year-Book separately? We believe they would have a large sale, whereas the price of the Year-Book must keep it out of reach of many practitioners who would be glad to own this work of reference. While the "Centrallblätter" keep us really up to date in the different branches, the Year-Book is always about six months behind; another factor which lessens its value to the busy and progressive student. He must get the last six months' information elsewhere.

We value the Year-Book and think the remarks of the collaborators of special importance in pointing out both good and bad work, or, better, in showing up errors of judgment. Such remarks should be of real service to younger practitioners who desire to write.

The profession at large should be sincerely grateful to Dr. Gould for the Year-Book, which is issued solely for the benefit of practitioners who are too busy to look up papers in which they may be interested, or too far distant from a good fountain of medical information to know what articles on any medical subject have lately appeared.

Essentials of Bacteriology. By M. V. BALL. (*W. B. Saunders, Philadelphia, Pa.*, 1897.)

Nothing in technical literature affords more depressing reading than a "compend," and the more widely removed the student from a practical acquaintance with the raw material out of which the subject itself is constructed, so much the more ineffective will be the efforts of any writer to provide him even temporarily with a short cut to knowledge Certain compends may perhaps be defended. In studying anatomy, for instance, the student has probably dissected, though perhaps more or less hurriedly, the whole or at least the greater part of the human body and has familiarized himself with the details, so that he has obtained a mental picture of the various organs and their relations. It is possible, then, that under these circumstances a compend may remind him of many half-forgotten facts, and he may retain this information until the emergency, represented by an examination, is over. But with the scanty opportunities afforded by most of our medical schools in this country for obtaining any adequate practical acquaintance with bacteriological methods, the need or advantage of a compend is hardly apparent. To any one who has had an opportunity of studying bacteriology in the only way in which it can be learned, namely, by practical work in the laboratory, the scope of the book is altogether too narrow to be of much service. To the student who has had no such opportunities it can have but little meaning, and even a word-for-word knowledge of its contents would hardly enable him to pass a properly conducted examination upon bacteriology.

The author acknowledges his indebtedness to several text-books dealing with the subject both in English and in foreign languages, but among his list we miss the names of some of the most trustworthy authorities. The definitions are terse, but not always free from obscurity or even error.

As a short text-book for the beginner, or as an aid in the case of the more advanced student to the revival of forgotten knowledge, any compend upon bacteriology must be found wanting.

In view, therefore, of the insuperable difficulties with which he has had to contend, the author must not be criticized too severely for shortcomings which are necessarily involved in the nature of the subject with which he has had to deal.

PUBLICATIONS OF THE JOHNS HOPKINS HOSPITAL.

THE JOHNS HOPKINS HOSPITAL REPORTS.

VOLUME I. 423 pages, 99 plates.

Report in Pathology.

The Vessels and Walls of the Dog's Stomach; A Study of the Intestinal Contraction; Healing of Intestinal Sutures; Reversal of the Intestine; The Contraction of the Vena Portae and its Influence upon the Circulation. By F. P. MALL, M. D.

A Contribution to the Pathology of the Gelatinous Type of Cerebellar Sclerosis (Atrophy). By HENRY J. BERKLEY, M. D.

Reticulated Tissue and its Relation to the Connective Tissue Fibrils. By F. P. MALL, M. D.

Report in Dermatology.

Two Cases of Protozoan (Coccidioidal) Infection of the Skin and other Organs. By T. C. GILCHRIST, M. D., and EMMET RIXFORD, M. D.

A Case of Blastomycetic Dermatitis in Man; Comparisons of the Two Varieties of Protozoa, and the Blastomyces found in the preceding Cases, with the so-called Parasites found in Various Lesions of the Skin, etc.; Two Cases of Molluscum Fibrosum; The Pathology of a Case of Dermatitis Herpetiformis (Duhring). By T. C. GILCHRIST, M. D.

Report in Pathology.

AN EXPERIMENTAL STUDY of the Thyroid Gland of Dogs, with especial consideration of Hypertrophy of this Gland. By W. S. HALSTED, M. D.

VOLUME II. 570 pages, with 28 plates and figures.

Report in Medicine.

On Fever of Hepatic Origin, particularly the Intermittent Pyrexia associated with Gallstones. By WILLIAM OSLER, M. D.

Some Remarks on Anomalies of the Uvula. By JOHN N. MACKENZIE, M. D.

On Pyrodin. By H. A. LAFLEUR, M. D.

Cases of Post-febrile Insanity. By WILLIAM OSLER, M. D.

Acute Tuberculosis in an Infant of Four Months. By HARRY TOULMIN, M. D.

Rare Forms of Cardiac Thrombi. By WILLIAM OSLER, M. D.

Notes on Endocarditis in Phthisis. By WILLIAM OSLER, M. D.

Report in Medicine.

Tubercular Peritonitis. By WILLIAM OSLER, M. D.

A Case of Raynaud's Disease. By H. M. THOMAS, M. D.

Acute Nephritis in Typhoid Fever. By WILLIAM OSLER, M. D.

Report in Gynecology.

The Gynecological Operating Room. By HOWARD A. KELLY, M. D.

The Laparotomies performed from October 16, 1889, to March 3, 1890. By HOWARD A. KELLY, M. D., and HUNTER ROBB, M. D.

The Report of the Autopsies in Two Cases Dying in the Gynecological Wards without Operation; Composite Temperature and Pulse Charts of Forty Cases of Abdominal Section. By HOWARD A. KELLY, M. D.

The Management of the Drainage Tube in Abdominal Section. By HUNTER ROBB, M. D.

The Gonococcus in Pyosalpinx; Tuberculosis of the Fallopian Tubes and Peritoneum; Ovarian Tumor; General Gynecological Operations from October 15, 1889, to March 4, 1890. By HOWARD A. KELLY, M. D.

Report of the Urinary Examination of Ninety-one Gynecological Cases. By HOWARD A. KELLY, M. D., and ALBERT A. GHRISKEY, M. D.

Ligature of the Trunks of the Uterine and Ovarian Arteries as a Means of Checking Hemorrhage from the Uterus, etc. By HOWARD A. KELLY, M. D.

Carcinoma of the Cervix Uteri in the Negress. By J. W. WILLIAMS, M. D.

Elephantiasis of the Clitoris. By HOWARD A. KELLY, M. D.

Myxo-Sarcoma of the Clitoris. By HUNTER ROBB, M. D.

Kolpo-Ureterotomy. Incision of the Ureter through the Vagina, for the treatment of Ureteral Stricture; Record of Deaths following Gynecological Operations. By HOWARD A. KELLY, M. D.

Report in Surgery, I.

The Treatment of Wounds with Especial Reference to the Value of the Blood Clot in the Management of Dead Spaces. By W. S. HALSTED, M. D.

Report in Neurology, I.

A Case of Chorea Insaniens. By HENRY J. BERKLEY, M. D.

Acute Angio-Neurotic Oedema. By CHARLES E. SIMON, M. D.

Haematomyelia. By AUGUST HOCH, M. D.

A Case of Cerebro-Spinal Syphilis, with an unusual Lesion in the Spinal Cord. By HENRY M. THOMAS, M. D.

Report in Pathology, I.

Amœbic Dysentery. By WILLIAM T. COUNCILMAN, M. D., and HENRI A. LAFLEUR, M. D.

VOLUME III. 766 pages, with 69 plates and figures.

Report in Pathology.

Papillomatous Tumors of the Ovary. By J. WHITRIDGE WILLIAMS, M. D.

Tuberculosis of the Female Generative Organs. By J. WHITRIDGE WILLIAMS, M. D.

Report in Pathology.

Multiple Lympho-Sarcomata, with a report of Two Cases. By SIMON FLEXNER, M. D.

The Cerebellar Cortex of the Dog. By HENRY J. BERKLEY, M. D.

A Case of Chronic Nephritis in a Cow. By W. T. COUNCILMAN, M. D.

Bacteria in their Relation to Vegetable Tissue. By H. L. RUSSELL, PH. D.

Heart Hypertrophy. By WM. T. HOWARD, JR., M. D.

Report in Gynecology.

The Gynecological Operating Room; An External Direct Method of Measuring the Conjugata Vera; Prolapsus Uteri without Diverticulum and with Anterior Enterocele; Lipoma of the Labium Majus; Deviations of the Rectum and Sigmoid Flexure associated with Constipation a Source of Error in Gynecological Diagnosis; Operation for the Suspension of the Retroflexed Uterus. By HOWARD A. KELLY, M. D.

Potassium Permanganate and Oxalic Acid as Germicides against the Pyogenic Cocci. By MARY SHERWOOD, M. D.

Intestinal Worms as a Complication in Abdominal Surgery. By A. L. STAVELY, M. D.

Gynecological Operations not involving Cœliotomy. By HOWARD A. KELLY, M. D. Tabulated by A. L. STAVELY, M. D.

The Employment of an Artificial Retroposition of the Uterus in covering Extensive Denuded Areas about the Pelvic Floor; Some Sources of Hemorrhage in Abdominal Pelvic Operations. By HOWARD A. KELLY, M. D.

Photography applied to Surgery. By A. S. MURRAY.

Traumatic Atresia of the Vagina with Hæmatokolpos and Hæmatometra. By HOWARD A. KELLY, M. D.

Urinalysis in Gynecology. By W. W. RUSSELL, M. D.

The Importance of employing Anæsthesia in the Diagnosis of Intra-Pelvic Gynecological Conditions. By HUNTER ROBB, M. D.

Resuscitation in Chloroform Asphyxia. By HOWARD A. KELLY, M. D.

One Hundred Cases of Ovariotomy performed on Women over Seventy Years of Age. By HOWARD A. KELLY, M. D., and MARY SHERWOOD, M. D.

Abdominal Operations performed in the Gynecological Department, from March 5, 1890, to December 17, 1892. By HOWARD A. KELLY, M. D.

Record of Deaths occurring in the Gynecological Department from June 6, 1890, to May 4, 1892.

VOLUME IV. 504 pages, 33 charts and illustrations.

Report on Typhoid Fever.

By WILLIAM OSLER, M. D., with additional papers by W. S. THAYER, M. D., and J. HEWETSON, M. D.

Report in Neurology.

Dementia Paralytica in the Negro Race; Studies in the Histology of the Liver; The Intrinsic Pulmonary Nerves in Mammalia; The Intrinsic Nerve Supply of the Cardiac Ventricles in Certain Vertebrates; The Intrinsic Nerves of the Submaxillary Gland of *Mus musculus*; The Intrinsic Nerves of the Thyroid Gland of the Dog; The Nerve Elements of the Pituitary Gland. By HENRY J. BERKLEY, M. D.

Report in Surgery.

The Results of Operations for the Cure of Cancer of the Breast, from June, 1889, to January, 1894. By W. S. HALSTED, M. D.

Report in Gynecology.

Hydrosalpinx, with a report of twenty-seven cases; Post-Operative Septic Peritonitis; Tuberculosis of the Endometrium. By T. S. CULLEN, M. B.

Report in Pathology.

Deciduoma Malignum. By J. WHITRIDGE WILLIAMS, M. D.

VOLUME V. 480 pages, with 32 charts and illustrations.

CONTENTS:

The Malarial Fevers of Baltimore. By W. S. THAYER, M. D., and J. HEWETSON, M. D.

A Study of some Fatal Cases of Malaria. By LEWELLYS F. BARKER, M. B.

Studies in Typhoid Fever.

By WILLIAM OSLER, M. D., with additional papers by G. BLUMER, M. D., SIMON FLEXNER, M. D., WALTER REED, M. D., and H. C. PARSONS, M. D.

VOLUME VI. 414 pages, with 79 plates and figures.

Report in Neurology.

Studies on the Lesions produced by the Action of Certain Poisons on the Cortical Nerve Cell (Studies Nos. I to V). By HENRY J. BERKLEY, M. D.

Introductory.—Recent Literature on the Pathology of Diseases of the Brain by the Chromate of Silver Methods; Part I.—Alcohol Poisoning.—Experimental Lesions produced by Chronic Alcoholic Poisoning (Ethyl Alcohol). 2. Experimental Lesions produced by Acute Alcoholic Poisoning (Ethyl Alcohol); Part II.—Serum Poisoning.—Experimental Lesions induced by the Action of the Dog's Serum on the Cortical Nerve Cell; Part III.—Ricin Poisoning.—Experimental Lesions induced by Acute Ricin Poisoning. 2. Experimental Lesions induced by Chronic Ricin Poisoning; Part IV.—Hydrophobic Toxaemia.—Lesions of the Cortical Nerve Cell produced by the Toxine of Experimental Rabies; Part V.—Pathological Alterations in the Nuclei and Nucleoli of Nerve Cells from the Effects of Alcohol and Ricin Intoxication; Nerve Fibre Terminal Apparatus; Asthenic Bulbar Paralysis. By HENRY J. BERKLEY, M. D.

Report in Pathology.

Fatal Puerperal Sepsis due to the Introduction of an Elm Tent. By THOMAS S. CULLEN, M. B.

Pregnancy in a Rudimentary Uterine Horn. Rupture, Death, Probable Migration of Ovum and Spermatozoa. By THOMAS S. CULLEN, M. B., and G. L. WILKINS, M. D.

Adeno-Myoma Uteri Diffusum Benignum. By THOMAS S. CULLEN, M. B.

A Bacteriological and Anatomical Study of the Summer Diarrhœas of Infants. By WILLIAM D. BOOKER, M. D.

The Pathology of Toxalbumin Intoxications. By SIMON FLEXNER, M. D.

The price of a set bound in cloth [Vols. I-VI] of the Hospital Reports is $30.00. Vols. I, II and III are not sold separately. The price of Vols. IV, V and VI is $5.00 each.

Monographs.

The following papers are reprinted from Vols. I, IV, V and VI of the Reports, for those who desire to purchase in this form:

STUDIES IN DERMATOLOGY. By T. C. GILCHRIST, M. D., and EMMET RIXFORD, M. D. 1 volume of 164 pages and 41 full-page plates. Price, bound in paper, $3.00.

THE MALARIAL FEVERS OF BALTIMORE. By W. S. THAYER, M. D., and J. HEWETSON, M. D. And A STUDY OF SOME FATAL CASES OF MALARIA. By LEWELLYS F. BARKER, M. B. 1 volume of 280 pages. Price, in paper, $2.75.

STUDIES IN TYPHOID FEVER. By WILLIAM OSLER, M. D., and others. Extracted from Vols. IV and V of the Johns Hopkins Hospital Reports. 1 volume of 481 pages. Price, bound in paper, $3.00.

THE PATHOLOGY OF TOXALBUMIN INTOXICATIONS. By Simon Flexner, M. D. 1 volume of 150 pages with 4 full-page lithographs. Price, bound in paper, $2.00.

Subscriptions for the above publications may be sent to

THE JOHNS HOPKINS PRESS, BALTIMORE, MD.

THE JOHNS HOPKINS MEDICAL SCHOOL. SESSION 1897-1898.

FACULTY.

DANIEL C. GILMAN, LL. D., President.
WILLIAM H. WELCH, M. D., LL. D., Dean and Professor of Pathology.
IRA REMSEN, M. D., Ph. D., LL. D., Professor of Chemistry.
WILLIAM OSLER, M. D., LL. D., F. R. C. P., Professor of the Principles and Practice of Medicine.
HENRY M. HURD, M. D., LL. D., Professor of Psychiatry.
WILLIAM S. HALSTED, M. D., Professor of Surgery.
HOWARD A. KELLY, M. D., Professor of Gynecology and Obstetrics.
FRANKLIN P. MALL, M. D., Professor of Anatomy.
JOHN J. ABEL, M. D., Professor of Pharmacology.
WILLIAM H. HOWELL, Ph. D., M. D., Professor of Physiology.
WILLIAM K. BROOKS, Ph. D., LL. D., Professor of Comparative Anatomy and Zoology.
JOHN S. BILLINGS, M. D., LL. D., Lecturer on the History and Literature of Medicine.
ALEXANDER C. ABBOTT, M. D., Lecturer on Hygiene.
CHARLES WARDELL STILES, Ph. D., M. S., Lecturer on Medical Zoology.
ROBERT FLETCHER, M. D., M. R. C. S., Lecturer on Forensic Medicine.
WILLIAM D. BOOKER, M. D., Clinical Professor of Diseases of Children.
JOHN N. MACKENZIE, M. D., Clinical Professor of Laryngology and Rhinology.
SAMUEL THEOBALD, M. D., Clinical Professor of Ophthalmology and Otology.
HENRY M. THOMAS, M. D., Clinical Professor of Diseases of the Nervous System.
SIMON FLEXNER, M. D., Associate Professor of Pathology.
J. WHITRIDGE WILLIAMS, M. D., Associate Professor of Obstetrics.
LEWELLYS F. BARKER, M. B., Associate Professor of Anatomy.
WILLIAM S. THAYER, M. D., Associate Professor of Medicine.
JOHN M. T. FINNEY, M. D., Associate Professor of Surgery.
GEORGE P. DREYER, Ph. D., Associate in Physiology.
WILLIAM W. RUSSELL, M. D., Associate in Gynecology.
HENRY J. BERKLEY, M. D., Associate in Neuro-Pathology.
J. WILLIAMS LORD, M. D., Associate in Dermatology and Instructor in Anatomy.
T. CASPAR GILCHRIST, M. R. C. S., Associate in Dermatology.
ROBERT L. RANDOLPH, M. D., Associate in Ophthalmology and Otology.
THOMAS B. ALDRICH, Ph. D., Associate in Physiological Chemistry.
THOMAS B. FUTCHER, M. B., Associate in Medicine.
JOSEPH C. BLOODGOOD, M. D., Associate in Surgery.
THOMAS S. CULLEN, M. B., Associate in Gynecology.
ROSS G. HARRISON, Ph. D., Associate in Anatomy.
FRANK R. SMITH, M. D., Instructor in Medicine.
GEORGE W. DORRIS, M. D., Assistant in Obstetrics.
WALTER JONES, Ph. D., Assistant in Physiological Chemistry.
ADOLPH G. HOEN, M. D., Instructor in Photo-Micrography.
SYDNEY M. CONE, M. D., Assistant in Surgical Pathology.
LOUIS E. LIVINGOOD, M. D., Assistant in Pathology.
HENRY BARTON JACOBS, M. D., Instructor in Medicine.
CHARLES R. BARDEEN, M. D., Assistant in Anatomy.
STEWART PATON, M. D., Assistant in Nervous Diseases.
NORMAN MCL. HARRIS, M. B., Assistant in Pathology.
HARVEY W. CUSHING, M. D., Assistant in Surgery.
J. M. LARNAR, M. D., Assistant in Clinical Microscopy.
J. L. WALS, Ph. G., Assistant in Pharmacy.

GENERAL STATEMENT.

The Medical Department of the Johns Hopkins University was opened for the instruction of students October, 1893. This School of Medicine is an integral and coördinate part of the Johns Hopkins University, and it also derives great advantages from its close affiliation with the Johns Hopkins Hospital.

The required period of study for the degree of Doctor of Medicine is four years. The academic year begins on the first of October and ends the middle of June, with short recesses at Christmas and Easter.

Men and women are admitted upon the same terms.

In the methods of instruction especial emphasis is laid upon practical work in the Laboratories and in the Dispensary and Wards of the Hospital. While the aim of the School is primarily to train practitioners of medicine and surgery, it is recognized that the medical art should rest upon a suitable preliminary education and upon thorough training in the medical sciences. The first two years of the course are devoted mainly to practical work, combined with demonstrations, recitations and, when deemed necessary, lectures, in the Laboratories of Anatomy, Physiology, Physiological Chemistry, Pharmacology and Toxicology, Pathology and Bacteriology. During the last two years the student is given abundant opportunity for the personal study of cases of disease, his time being spent largely in the Hospital Wards and Dispensary and in the Clinical Laboratories. Especially advantageous for thorough clinical training are the arrangements by which the students, divided into groups, engage in practical work in the Dispensary, and throughout the fourth year serve as clinical clerks and surgical dressers in the wards of the Hospital.

REQUIREMENTS FOR ADMISSION.

As candidates for the degree of Doctor of Medicine the school receives:

1. Those who have satisfactorily completed the Chemical-Biological course which leads to the A. B. degree in this university.

2. Graduates of approved colleges or scientific schools who can furnish evidence: (*a*) That they have acquaintance with Latin and a good reading knowledge of French and German; (*b*) That they have such knowledge of physics, chemistry, and biology as is imparted by the regular minor courses given in these subjects in this university.

The phrase "a minor course," as here employed, means a course that requires a year for its completion. In physics, four class-room exercises and three hours a week in the laboratory are required; in chemistry and biology, four class-room exercises and five hours a week in the laboratory in each subject.

3. Those who give evidence by examination that they possess the general education implied by a degree in arts or in science from an approved college or scientific school, and the knowledge of French, German, Latin, physics, chemistry, and biology above indicated.

Applicants for admission will receive blanks to be filled out relating to their previous courses of study.

They are required to furnish certificates from officers of the colleges or scientific schools where they have studied, as to the courses pursued in physics, chemistry, and biology. If such certificates are satisfactory, no examination in these subjects will be required from those who possess a degree in arts or science from an approved college or scientific school.

Candidates who have not received a degree in arts or in science from an approved college or scientific school, will be required (1) to pass, at the beginning of the session in October, the matriculation examination for admission to the collegiate department of the Johns Hopkins University, (2) then to pass examinations equivalent to those taken by students completing the Chemical-Biological course which leads to the A. B. degree in this University, and (3) to furnish satisfactory certificates that they have had the requisite laboratory training as specified above. It is expected that only in very rare instances will applicants who do not possess a degree in arts or science be able to meet these requirements for admission.

Hearers and special workers, not candidates for a degree, will be received at the discretion of the Faculty.

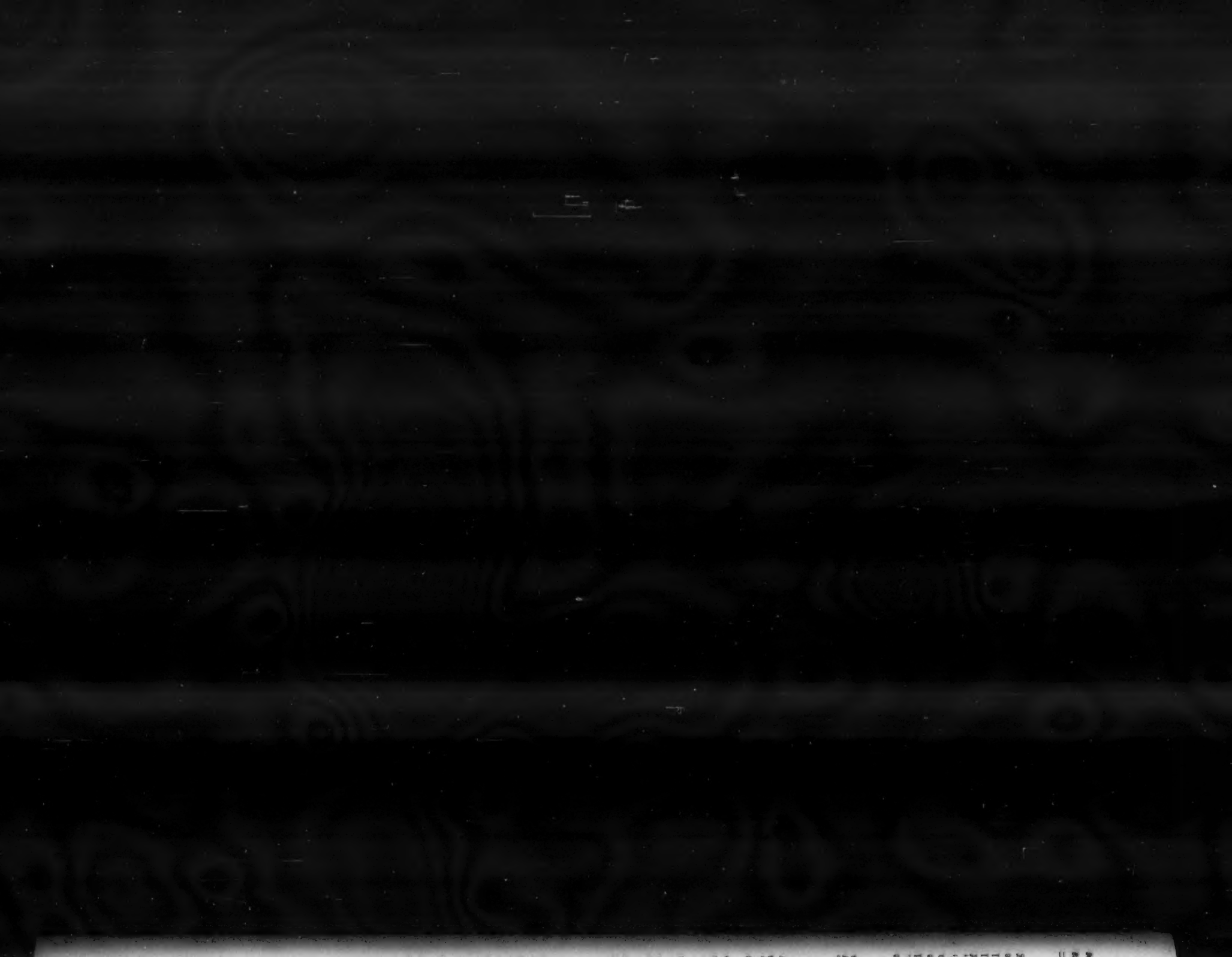
ADMISSION TO ADVANCED STANDING.

Applicants for admission to advanced standing must furnish evidence (1) that the foregoing terms of admission as regards preliminary training have been fulfilled, (2) that courses equivalent in kind and amount to those given here, preceding that year of the course for admission to which application is made, have been satisfactorily completed, and (3) must pass examinations at the beginning of the session in October in all the subjects that have been already pursued by the class to which admission is sought. Certificates of standing elsewhere cannot be accepted in place of these examinations.

SPECIAL COURSES FOR GRADUATES IN MEDICINE.

Since the opening of the Johns Hopkins Hospital in 1889, courses of instruction have been offered to graduates in medicine. The attendance upon these courses has steadily increased with each succeeding year and indicates gratifying appreciation of the special advantages here afforded. With the completed organization of the Medical School, it was found necessary to give the courses intended especially for physicians at a later period of the academic year than that hitherto selected. It is, however, believed that the period now chosen for this purpose is more convenient for the majority of those desiring to take the courses than the former one. The special courses of instruction for graduates in medicine are now given annually during the months of May and June. During April there is a preliminary course in Normal Histology. These courses are in Pathology, Bacteriology, Clinical Microscopy, General Medicine, Surgery, Gynecology, Dermatology, Diseases of Children, Diseases of the Nervous System, Genito-Urinary Diseases, Laryngology and Rhinology, and Ophthalmology and Otology. The instruction is intended to meet the requirements of practitioners of medicine, and is almost wholly of a practical character. It includes laboratory courses, demonstrations, bedside teaching, and clinical instruction in the wards, dispensary, amphitheatre, and operating rooms of the Hospital. These courses are open to those who have taken a medical degree and who give evidence satisfactory to the several instructors that they are prepared to profit by the opportunities here offered. The number of students who can be accommodated in some of the practical courses is necessarily limited. For these the places are assigned according to the date of application.

The Annual Announcement and Catalogue will be sent upon application. Inquiries should be addressed to the

REGISTRAR OF THE JOHNS HOPKINS MEDICAL SCHOOL, BALTIMORE.

The Johns Hopkins Hospital Bulletins are issued monthly. They are printed by THE FRIEDENWALD CO., Baltimore. Single copies may be procured from Messrs. CUSHING & CO. and the BALTIMORE NEWS COMPANY, Baltimore. Subscriptions, $1.00 a year, may be addressed to the publishers, THE JOHNS HOPKINS PRESS, BALTIMORE; single copies will be sent by mail for fifteen cents each.